(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 328 421**
A2

(12) # EUROPEAN PATENT APPLICATION

(21) Application number: **89301349.0**

(22) Date of filing: **13.02.89**

(51) Int. Cl.[4]: **A 61 L 29/00**
A 61 L 31/00, A 61 L 27/00,
A 61 L 15/03, A 61 L 17/00

(30) Priority: **11.02.88 US 154920 14.10.88 US 258189**

(43) Date of publication of application:
16.08.89 Bulletin 89/33

(84) Designated Contracting States:
AT BE CH DE FR GB IT LI NL SE

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An unreadable (Unreadable) part(s) of the originally filed application documents has (have) been excluded from the publication.

(54) **Infection-resistant compositions, medical devices and surfaces and methods for preparing and using same.**

(57) A method of preparing an infection-resistant medical device comprising one or more matrix-forming polymers selected from the group consisting of biomedical polyurethane, biomedical silicones and biodegradable polymers, and antimicrobial agents, especially a synergistic combination of a silver salt and chlorhexidine (or its salts); also disclosed are medical devices having the synergistic composition therein or compositions thereon.

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Description

Infection-Resistant Compositions, Medical Devices and Surfaces and Methods for Preparing and Using Same

Background of the Invention

The present invention relates to infection-resistance compositions, medical devices and surfaces and to methods for using and preparing the same. This application is a continuation-in-part of U.S. Patent Application Serial No. 254,920, filed February 11, 1988.

Medical devices for use externally or internally with humans or animals can serve to introduce bacterial, viral, fungal or other undesirable infections. Certain prior art devices become unworkable after a short period of time, and must be replaced. In the case of urinary catheters, for example, frequent replacement can cause excessive discomfort to the patient and prolonged hospitalization. In the case of intravenous catheters used for critical care patients, infections can themselves prove life threatening. Additionally, there is always a threat of exposure to infectious contamination from surfaces that contact patients, from surgical gloves, and from other medical gear and apparatus.

To prevent such contamination, medical devices can be treated with an antimicrobial agent. Known methods of preparing an infection-resistant medical device have been proposed in U.S. Patents Nos. 3,566,874, 3,674,901, 3,695,921, 3,705,938, 3,987,797, 4,024,871, 4,318,947, 4,381,380, 4,539,234, and 4,612,337.

In addition, antimicrobial compositions useful as coatings for medical devices or for forming the device itself are disclosed in U.S. Patents Nos. 3,699,956, 4,054,139, 4,592,920, 4,603,152, and 4,667,143. However, such known methods are somewhat complicated or deficient in the results obtained. The art has great need for medical devices which are able to resist microbial infection when placed in the area of the body to which it is applied and which provide this resistance over the period of time which it remains in place. At the same time, these desirable characteristics must be achieved without sacrifice of other well recognized desirable characteristics. In the case of catheters, for example, it is important that any coating thereon leave a surface which provides a minimum of resistance to insertion of the catheter and which does not release a toxic substance to be adsorbed by the body.

Furthermore, some uses of antimicrobial metal compounds including silver salts in antimicrobial coatings for medical devices are known. Also, chlorhexidine and its salts are known to be powerful antiseptics, but the combination of chlorhexidine with silver nitrate has been shown to have prophylactic properties in burn therapy. In addition, the combination of chlorhexidine and sulfadiazine is known in topical applications to exhibit synergism against strains of Pseudomonas, Proteus, and Staphylococcus, as disclosed in Quesnel et al, Synergism between Chlorhexidine and Sulphadiazine, Journal of Applied Bacteriology, 1978, 45, 397-405.

Summary of the Invention

A principal object of the present invention is to provide an improved method of preparing an infection-resistant medical device which will impart antimicrobial activity to the medical device through a sustained and controlled activity rate over an appreciable period of time, without hampering the biocompatibility of the surface and other intended functions of the device. A further object of the present invention is to provide an infection- resistant medical device having superior antimicrobial properties.

Still another object of the present invention is to provide an antimicrobial composition useful in providing an antimicrobial coating on medical devices.

In accordance with the first embodiment of the present invention, there is provided a method of preparing an infection-resistant medical device which comprises

(a) preparing a coating vehicle by dissolving a matric-forming polymer selected from the group consisting of biomedical polyurethane, biomedical silicones, biodegradable polymers and combinations thereof in at least one solvent therefor;

(b) incorporating at least one antimicrobial agent in the coating vehicle to form a coating composition;

(c) coating a medical device with the coating composition; and

(d) drying the coating medical device.

It is preferred in the first embodiment that the antimicrobial agent be a combination of a silver salt and a biguanide and further preferred that the antimicrobial agent be a combination of a silver salt and a member of the group consisting of chlorhexidine and its salts. Also useful are chlorhexidine alone or in combination with nonoxynol 9, or pipracil as well as silver sulfadiazine in combination with nonoxynol 9.

In accordance with a second embodiment of the present invention, there is provided an antimicrobial composition comprising a mixture of (a) chlorhexidine and its salts, and (b) a silver salt.

Further, in accordance with a second embodiment of the present invention there is provided a method of preparing an infection-resistant medical device which comprises incorporating thereon or therein an antimicrobial agent comprising (a) a member of the group consisting of chlorhexidine and its salts, and (b) a member of the group consisting of silver and its salts.

The second embodiment of the present invention further provides an infection-resistant medical device having a coating thereon comprising (a) a member of the group consisting of chlorhexidine and its salts, and (b) a member of the group consisting of silver and its salts.

Another embodiment of the present invention still further provides a method for coating a medical device to provide an infection-resistant coating thereon which comprises the steps of:

(a) dissolving a matrix-forming polymer in a solvent therefor;

(b) dissolving an antimicrobial agent selected from the group consisting of chlorhexidine and its salts in a solvent which is miscible with the solvent polymer mixture prepared in step (a);

(c) dispersing a silver salt in one of the solutions prepared in (a) or (b);

(d) combining the solvent solutions and dispersions prepared in steps (a), (b) and (c) to provide a coating vehicle;

(e) applying the coating vehicle to the surface of the medical device; and

(f) drying the coated medical device.

In addition, the present invention provides an antimicrobial composition useful in applying an infection-resistant coating to medical devices which, in use, will exhibit a sustained activity rate over an appreciable time period.

Detailed Description of the Invention

Surfaces which may embody the present invention can be generally any surfaces that contact patients or are important in health care, including table tops, hospital beds and various specific medical devices. Medical devices are those for use both externally and internally and include, for example, urinary, both internal and external, and intravenous catheters, contraceptives such as condoms, medical gloves, such as surgical and examination gloves, wound dressings, drainage tubes, orthopedic, penile and other implants, wound clips, sutures, hernia patches and arterial grafts. The devices or surfaces, sometimes generally together referred to as "surfaces" herein, can be made of a variety of natural or synthetic materials such as metals, plastics and polymers, and including Dacron®, rubber, latex, collagenous substances, silicone, polyurethane, polyvinyl chloride, Teflon®, polypropylene, polyethylene, poly(lactic acid), polyglycolic acid, cotton, silk, stainless steel, porous ceramics, and porcelain.

Definitions

The following specification refers to a number of microorganisms in describing the invention or its use. Unless otherwise stated, the following are the generally recognized names of the microorganisms, together with their source:

Organism	Source
Staphylococcus aureus	clinical isolate-Columbia Presbyterian Hosptial New York, New York
Staphylococcus epidermidis	clinical isolate-Columbia Presbyterian Hosptial New York, New York
Esherichia coli	clinical isolate-Columbia Presbyterian Hosptial New York, New York
Candida albicans	ATCC No. 11651

It is also noted that unless otherwise stated, the concentrations and ranges expressed as percentages (5), indicates the respective value based on weight of solid per volume of solvent. As an example, a 1% polyurethane in a solvent coating vehicle comprising tetrahydrofuran (THF) represents 1 gram of polyurethane in 100 ml of THF. On the other hand, in expressing relative proportions of two or more solvents in a coating vehicle, the percentages given are on a vol/vol basis.

Polymeric Coating Agent

The polymeric coating agent component of the coating vehicle of the present invention is selected from the group consisting of biomedical polyurethanes, biomedical silicones, biodegradable polymers and combinations thereof. It has been found that these particular polymeric materials enable the antimicrobial agent of the second embodiment of the invention to be retained and released in an active state on the coated medical device over an appreciable period of time, e.g., from about 12 to in excess of 21 days.

Selection of the coating vehicle depends upon the specific composition of the surface of the device to be coated, and the characteristics sought. For example, a polyurethane catheter is preferably coated with a formulation based on a biomedical polyurethane matrix-forming material. A silicone rubber catheter, on the other hand, preferably is provided with a coating having a silicone rubber as a matrix-forming material. It has

also been discovered that a final thin coat of a silicone fluid after a first coating of biomedical polyurethane or of silicone rubber imparts surface glossiness and lubricity to the catheter. Thus, multiple, combined coatings, described in greater detail below, can also be achieved with improved characteristics.

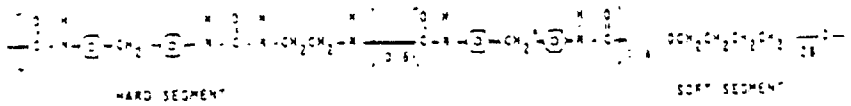
In addition to polymeric coating compositions, the antimicrobial compositions of this invention may be applied to surfaces of medical devices in powder form, preferably under conditions which cause adherence of the powder to the surface of the device. For example, medical gloves, such as surgical or examination gloves fabricated from latex, polyurethane or polyvinyl acetate, may be coated with a powder containing the antimicrobial composition, as will be explained below in more detail.

A. Biomedical Polyurethane

In accordance with the first embodiment of the invention, the essential polymeric coating agent component of the coating vehicle is biomedical polyurethane, since it has been found unexpectedly that polymeric materials of this class enable the antimicrobial agent to be retained in an active state on the coated medical device and released over an appreciable period of time, e.g., from about 12 to in excess of 21 days, without altering the biocompatibility, lubricity and non-thrombogenicity of the surface. Suitable biomedical polyurethanes include both the ether-based polyurethanes and the ester-based polyurethanes described on pages 175-177 of Controlled Release of Biologically Active Agents, by Richard W. Baker, John Wiley and Sons, 1987; the ether-based compounds are preferred. A thorough discussion of a number of proprietary biomedical polyurethanes is found in Polyurethanes in Medicine, by Michael D. Lelah and Stuart L. Cooper, CRC Press, Inc., Fla 1986, pp. 57-67.

The following is a listing of proprietary biomedical polyurethanes that are useful in accordance with the invention:

1. Biomer®, which consists of 4,4'-diphenylmethane-diisocyanate (MDI) and low molecular weight polytetramethyleneoxide (PTMO) segments with diamines as chain extenders. A proposed repeat unit chemical structure for Solution Grade Biomer® is:



2. Acuthane® is a block copolymer which contains 10% polymethylsiloxane and 90% polyetherurethane.

3. Pellethane® is an aromatic ether polyurethane. Pellethane® 2363 (80AE) is not crosslinked and is readily soluble in dimethylacetamide, tetrahydrofuran, or N-ethyl pyrrolidone. The 90A of the same series contains crosslinks due to the excess of isocyanates present during the polymerization process and is therefore more difficult to solubilize.

4. Rimplast® is a silicone urethane made with either aliphatic or aromatic ethers or esters of polyurethane and a reactive, high molecular weight silicone to form an interpenetrating network (IPN).

We have found that best results are obtained using Pellethane® 2363-80AE, one of a series of thermoplastic, segmented elastomers sold under the designation Pellethane® by Dow Chemical Co. These materials are described at p. 60 of Lelah et al, supra. Another suitable product is Biomer®, which is conveniently available as a 30 wt.% solution in N, N-dimethylacetamide (DMAC) described at pp. 57-58 of Lelah et al, supra. Another suitable material is Rimplast®, a series of biomedical urethanes containing silicones, reacted to form a series of interpenetrating network modified silicones containing polyurethanes. A description of these materials are found on pp. 61-63 of Lelah et al, supra.

The prior art, such as U.S. 4,667,143, fails to distinguish between various polymeric coating agents. The patent states that any one of a long list of resins may be mixed with an antimicrobial metal compound to provide antimicrobial coatings on medical devices. The working examples of the patent utilize either ABS polymers or alkoxy curing RTV silicone rubbers. Quite unexpectedly we have found that the specific application of biomedical polyurethanes as a coating agent is superior to all other known polymeric coating materials. This discovery was made by first determining the relative solubilities of various polymeric coating agents in equal amounts of DMAC and ethylacetate. The results of this screening test are shown in Table I.

TABLE I

Solubility of Various Polymers in Solvent Comprising 50% DMAC + 50% Ethyl Acetate

1.	POLY (ETHYLENE)	NS
2.	POLY (METHYL METHACRYLATE)	S
3.	POLY (ETHYLENE-MALEIC ANHYDRIDE)	NS
4.	POLY (CAPROLACTONE)	S
5.	POLY (VINYL ALCOHOL) MW 25,000	NS
6.	POLY-3-HYDROXYBUTYRATE $5x10^5$	NS
7.	POLY (ETHYLENE OXIDE) MW 4,000,000	NS
8.	POLY (BUTANEDIOL-1, 4-TERE-PHTHALATE)	NS
9.	POLY (HEXAMETHYLENE DODECANEDIAMIDE) NYLON	NS
10.	POLY (VINYL ACETATE) MW 500,000	S
11.	POLY (VILIDENE CHLORIDE-ACRYLONITRILE) 80:20	S
12.	POLY (HEXAMETHYLENE SEBACAMIDE) NYLON	NS
13.	POLY (PROPYLENE, ISOTACTIC)	NS
14.	POLY (ETHYL METHACRYLATE)	S
15.	POLY (STYRENE-MALEIC ANHYDRIDE)	S
16.	POLY (STYRENE ALLYL ALCOHOL)	S
17.	POLYACRYLAMIDE	NS
18.	POLY (ISO-BUTYL METHACRYLATE)	S
19.	POLY (VINYL PYRROLIDONE)	S
20.	POLY (PROPYLENE, CHLORINATED, 65%)	S
21.	POLY (N-BUTYL METHACRYLATE-ISO-BUTYL METHACRYLATE 50/50)	S
22.	POLY (VINYL CHLORIDE-VINYL ACETATE)	S
23.	POLY (ACRYLIC ACID) MW 4,000,000	NS
24.	POLY (HEXAMETHYLENE ADIPAMIDE)	NS
25.	POLY (N-BUTYL METHACRYLATE)	S
26.	POLY (CARBONATE BISPHENOL A)	NS
27.	POLY (LAURYL LACTIM)	NS
28.	POLY (CAPROLACTAM)	NS
29.	POLY (ACRYLAMIDE-ACRYLIC ACID SODIUM SALT) 70% CARBOXYL HIGH CARBOXYL MW 200,000	NS
30.	POLY (VINYL ALCOHOL) 88% MOLE HYDROLYZED, MW 25,000	NS
31.	POLY (ACETAL) RESIN	NS
32.	POLY (STYRENE-ACRYLONITRILE 75:25)	S
33.	POLY (METHYL VINYL ETHER/MALEIC ANHYDRIDE)	NS
34.	POLY (SULFONE) RESIN	S
35.	POLY (VINYLDIENE FLUORIDE)	S
36.	POLY (TETRAFLUOROETHYLENE)	NS
37.	POLY (VINYLDIENE CHLORIDE/VINYL CHLORIDE 86:12)	S
38.	POLY (VINYL BUTYRAL) MW 100,000-150,000	S
39.	POLY (p-VINYL PHENOL)	S
40.	POLY (ETHYLENE-ACRYLIC ACID 92:8)	NS
41.	POLYURETHANE (DOW PELLETHANE® 2363-80AE)	S

S = READILY SOLUBLE NS - NOT SOLUBLE

After rejecting the insoluble polymers, steps were taken to coat the soluble polymers, i.e., those identified in Table I as numbers 2, 4, 10, 11, 14, 15, 16, 18, 19, 20, 21, 22, 25, 32, 34, 35, 37, 38, 39, and 41, upon catheters to determine which formed stable, workable coatings. Both urinary and I.V. catheters were used, and for this test, the urinary catheter was fabricated of latex and the I.V. catheter of Pellethane® 2363, 90A, described above.

Two different coating formulations were used having the following formulations:

1. 1% chlorhexidine acetate (CHA) + 6% polymer in a solvent consisting of 50% DMAC + 50% ethyl acetate (EA)
2. 2% CHA + 6% polymer in a solvent consisting of 50% DMAC + 50% EA

The key characteristics of glossiness, smoothness, and stickiness of the exposed coating surface as well as the degree of adhesion of the coating to the catheters surfaces of the coated polymers were then compared, and the results are shown in Table II.

TABLE II

Quality of Coating on the Polyurethane Catheter (I.V.) and the Latex (URO) Urinary Catheter

	IV GLOSSINESS	URO GLOSSINESS	IV SMOOTHNESS	URO SMOOTHNESS	IV STICKINESS	URO STICKINESS	IV ADHESION	URO ADHESION
2	YES	YES	YES	YES	SLIGHT	YES	GOOD	POOR
4	SEMI	SEMI	YES	YES	NO	NO	GOOD	GOOD
10	YES	YES	YES	YES	NO	NO	GOOD	POOR
11	SEMI	SEMI	NO	NO	NO	NO	GOOD	POOR
14	SEMI	SEMI	YES	YES	SLIGHT	NO	GOOD	POOR
15	YES	YES	YES	YES	NO	NO	GOOD	GOOD
16	YES	YES	YES	YES	NO	NO	GOOD	GOOD
18	NO	NO	YES	YES	NO	NO	GOOD	GOOD
19	YES	YES	YES	YES	YES	YES	GOOD	GOOD
20	SEMI	NO	YES	YES	SLIGHT	NO	GOOD	GOOD
21	NO	NO	YES	YES	SLIGHT	NO	GOOD	GOOD
22	YES	YES	YES	YES	YES	NO	GOOD	POOR
25	NO	NO	YES	YES	YES	NO	GOOD	GOOD
32	YES	YES	YES	YES	YES	NO	GOOD	POOR
34	NO	NO	MEDIUM	YES	NO	SLIGHT	GOOD	POOR
35	NO	NO	YES	YES	YES	YES	GOOD	POOR
37	SEMI	NO	YES	MEDIUM SMOOTH	YES	YES	GOOD	FAIR
38	NO	SEMI	NO	YES	YES	YES	GOOD	POOR
39	YES	SEMI	YES	YES	SLIGHT	NO	GOOD	GOOD
41	YES	YES	YES	YES	NO	NO	GOOD	GOOD

Coating Formulas: URO = 6% Polymer + 1% CHA in $\frac{50}{50}$

I.V. = 6% Polymer + 2% CHA in $\frac{50}{50}$

Thus, although several polymers can be used as controlled delivery matrices, biomedical polyurethane, number 41 in Table II, was found to possess across-the-board superior characteristics.

Glossiness, smoothness, and stickiness of the exposed coating surface as well as adhesion of the coating to the device are crucial characteristics. Equally important to the invention is the coating agent's ability to absorb and release, in a controlled-dosing manner, bio-active agents. Again, biomedical polyurethane was far superior, and the results are shown in Table III, below. For this comparison, chlorhexidine diacetate (CHA) was incorporated into solutions of each of the polymers found to be soluble as listed in Table I.

TABLE III

Comparative Matrices Days of Activity

POLYMER MATRIX SYSTEM	I.V.	URO
1. POLY (METHYL METHACRYLATE)	3	NT
2. POLY (CAPROLACTONE)	3	NT
3. POLY (VINYL ACETATE) MW=500,000	2	NT
4. POLY (VINYLDIENE CHLORIDE-ACRYLONITRILE) 80:20	1	NT
5. POLY (ETHYL METHACRYLATE)	2	NT
6. POLY (STYRENE-MALEIC ANHYDRIDE)	0	0
7. POLY (STYRENE ALLYL ALCOHOL)	1	1
8. POLY (ISO-BUTYL METHACRYLATE)	2	2
9. POLY (VINYL PYRROLIDONE)	2	2
10. POLY (PROPYLENE, CHLORINATED, 65%)	2	2
11. POLY (N-BUTYL METHACRYLATE-ISO-BUTYL METHACRYLATE) 50/50	2	2
12. POLY (VINYL CHLORIDE-VINYL ACETATE)	2	NT
13. POLY (N-BUTYL METHACRYLATE)	1	2
14. POLY (STYRENE-ACRYLONITRILE 75:25)	2	NT
15. POLY (SULFONE) RESIN	1	NT
16. POLY (VINYLDIENE FLUORIDE)	1	NT
17. POLY (VINYLDIENE CHLORIDE/VINYL CHLORIDE) 88:12	1	2
18. POLY (VINYL BUTYRAL) MW=100,000-150,000	3	NT
19. POLY (p-VINYL PHENOL)	1	0
20. POLY (URETHANE) DOW PELLETHANE®	>4	>4
21. PTUE 205 RIMPLAST®	3	3

I.V. = intravenous catheter fabricated of Pellethane® 2363, 90A

URO = urinary catheter fabricated of latex

NT = not tested due to poor film formation or lack of adhesion of coating to substrate.

The coating formulas used in preparing coating vehicles for Table III were:

1. Urinary Catheters: 1% CHA + 6% Polymer in solvent.
2. I.V. Catheters: 2% CHA + 6% Polymer in solvent.

In both cases, the solvent consisted of 50% dimethylacetamide and 50% ethyl acetate.

The results given in Table III were obtained using the following bioassay:

1. Latex Urinary Catheters: 2 cm. sections were soaked in 5cc of Trypticase Soy Broth (TSB) and challenged with 10^4 CFU of a 1:1 mixture of Staph. epidermidis and E. coli pre-diluted to 0.3 optical density at 600 nm.
2. Polyurethane I.V. Catheters: 2cm. sections thereof were soaked as above and challenged with 10^4 CFU of Staph. aureus, again pre-diluted to 0.3 optical density at 600 nm.

This was a severe test, where the catheters were challenged daily with a broth culture having 10^4 CFU of the bacteria. The results show superior performance of biomedical polyurethane in maintaining sustained activity for more than four days for both types of catheters when coated with Pellethane® 2363 (line 21) and three days for Rimplast® PTUE 205, a silicone IPN modified urethane. The other resins averaged only one to two days.

The superior characteristics of the biomedical polyurethanes, lines 20 and 21, are surprising, since the prior art does not hint or suggest that any one of the above polymer matrices is any better than any other. Instead, the art teaches a general and uniform performance from each.

As a consequence of these results, several factors are postulated to account for the superior performance of biomedical polyurethane.

Polymer Backbone Rotational Flexibility:

It is well established that apart from the molecular weight of a solute, solubility in a polymer depends on the ability of the backbone of that polymer to rotate about one or more axes. Polyurethane's backbone flexibility falls somewhere in between the extreme freedom of rotation found in the silicone rubbers to the inflexibility of polystyrene. Since polyurethane is a segmented block copolymer made of both hard and soft segments it combines the ability of readily releasing bio-active agents from the amorphous phase with the slow release, reservoir-like characteristics of the hard or crystalline domain. Intramatrix diffusion probably occurs as the bio-active drug levels in the soft domains drop, causing a gradient related flow of solute out of the crystalline phase into the more flexible areas which then in turn diffuses out into the environment.

Progressive Formation of Interconnected Diffusion Channels:

As the drug molecules at the surface of the matrix are dissolved, the solute (blood, perspiration, saline, media etc.) is allowed to penetrate into the film, thus forming micro-channels which further facilitate the release process. The pore formation is likely proportional to the flexibility of the backbone of the polymer, whereby the rate of channeling falls as the domain becomes more crystalline.

Polyurethane has, on the average, 75 to 100 times the water absorption of silicone (RTV) and 25 times that of polystyrene. The greater value for polyurethane is probably due to the hydrophilic nature of the soft segment and presumably means that channel formation is enhanced.

Electrical Properties of the Matrix:

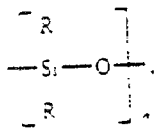
The charge that a polymer carries influence the affinity of the antimicrobial agent for the matrix. In some cases, such as when the antimicrobial agents silver (Ag) or chlorhexidine acetate (CHA) are mixed with latex, the binding is so strong that ions of the antimicrobial agent are restricted in their ability to diffuse out of the matrix. Some biomedical polyurethanes carry a positive charge and therefore do not react with, and thus inactivate, cationic antimicrobial agents such as Ag or CHA. Anionic compounds such as piperacillin or sulfadiazine are relatively unreactive and extremely soluble so that they do not bind to polyurethane and are released at a steady and prolonged rate.

Thus, the polymeric coating agent component cannot be polyethylene vinyl acetate, polyvinyl chloride or polyvinyl alcohol, because such polymers give unsatisfactory results. As mentioned above, the polymer of choice is a polyether polyurethane and, more specifically, Pellathane® 2363-80AE. It has been further found that this polymer in solvent must critically range from 1-10%, and preferably 2-6%, and most preferably 3% by volume, for best performance.

B. Biomedical Silicones

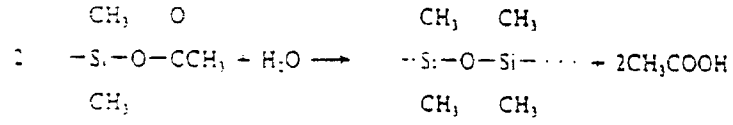
Suitable biomedical silicones include the silicone rubbers or elastomers described on pp. 156-162 of Controlled Release of Biologically Active Agents, by Richard W. Baker, John Wiley and Sons, 1987.

Silicone rubbers having the general formula

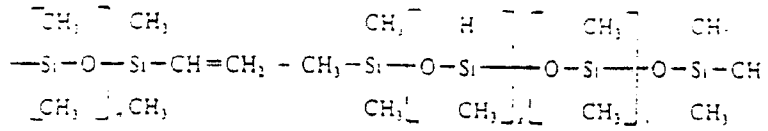


where R is either a methyl of a $-C_6H_6$ substituent, are useful. More specifically, the following proprietary biomedical silicones may be used:

1. Silastic® Type A Medical Adhesive, a polydimethyl siloxane sold by Dow Corning and which is a one component system which cures at ambient room temperature and humidity. Its formula is:

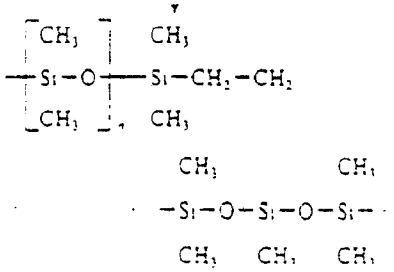


2. Other Silastic® products that can be used to form time release matrices include:
   (a) Q72213 - a medical grade dispersion of silicone in trichloroethane;
   (b) Silastic® 360; and
   (c) MDX4-4159, a proprietary product of Dow Corning containing 50% of an amino functional polydimethyl siloxane copolymer and 50% of mixed aliphatic and isopropanol solvents.
3. Two component vinyl curing silicone - a dimethyl silicone compound with a vinyl terminated prepolymer component is reacted to the backbone of a second silicone component.

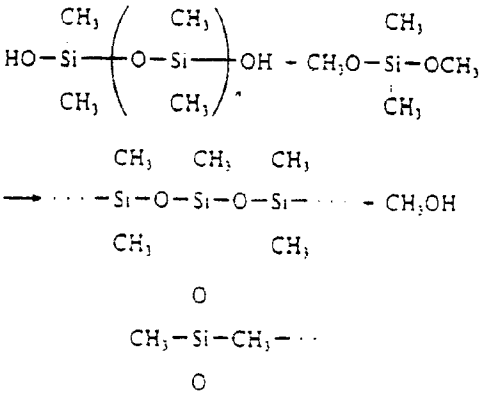


Vinyl-terminated silicone plus catalyst (prepolymer)

Methyl hydrogen silicone (curing compound)



4. Two component curing silicone - Silastic® 382 is an example of a silicone which cures by condensation whereby a prepolymer containing a hydroxy group is crosslinked by the addition of a methoxysilane and catalyst.



It is preferred to employ room temperature curing materials. It is also preferred to employ a mixture of equal parts of a polydimethyl siloxane such as Silastic® Type A adhesive and a mixed amino functional polydimethyl siloxane copolymer such MDX4-4159 in mixed aliphatic and isopropanol solvents, to provide a coating surface having a smooth surface and extended period of activity.

The selection of specific polymeric coating agent to form a coating matrix will depend upon the nature of the surface to which the coating will be applied. It is preferred that a biomedical polyurethane be applied to a polyurethane surface to assure good coating adherence. A biomedical silicone, such as a mixture of Silastic® Type A Medical Adhesive and MDX4-4159, is suitable to coat a device that is fabricated of silicone, polyurethane of of latex.

C. Biodegradable Polymers

It has further been found that use of a biodegradable polymer in the coating composition of this invention, either alone or in combination with one or more of the other biomedical polymers, enhances the character of the polymer matrix. Suitable biodegradable polymers include the homopolymers poly(glycolic acid), poly(D-lactic acid), poly(D,L-lactic acid), poly(D,L-ethylglycolic acid), poly(dimethylglycolic acid), poly(D, L-methylethylglycolic acid), and poly(E-caprolactone), as well as biodegradable polyhydroxy butyric acid and mixtures thereof. A preferred biodegradable polymer is polylactic acid (PLA).

Thus biodegradable polymer may be added to biomedical polyurethane in the quantities indicated herein. The biodegradable polymer modulates the rate of release of antimicrobial drugs. The initial burst of drug which occurs during the first few days after implantation is more or less eliminated since the drug is bound in the biodegradable polymer and will be released only when degradation of the polymer occurs. Inclusion of a biodegradable polymer such as PLA in the matrix gives prolonged biocidal activity as confirmed in in vitro studies, shown in Table IV, below.

TABLE IV

Enhanced Efficacy of Polyurethane + PLA Matrix

Coating Composition	Days of Activity*
1. 3% DPU + 3% CHA	4
2. 3% DPU + 1% PLA + 3% CHA	6
3. 3% DPU + 1% AgSD + 1% CHA	4
4. 3% DPU + 1% PLA + 1% AgSD + 1% CHA	5

DPU = Pellethane® 2363-80AE - Dow Chemical Co.

PLA = poly (lactic acid) molecular weight of 100000

AgSD = silver sulfadiazine

CHA = chlorhexidine diacetate

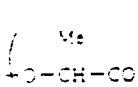
Solvent = 25 parts of ethanol and 75 parts of tetrahydrofuran (THF)

* determined according to the bioassay set forth above with regard to Table III

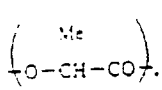
An additional advantage of using a biodegradable polymer such as PLA in a polyurethane matrix is to allow improved tissue ingrowth simultaneously with a prolonged antimicrobial effect as the biodegradable polymer degrades. Thus, this embodiment of the invention is particularly important in orthopedic applications as well as in such devices as arterial grafts where there is a need for formation of the pseudo-intima or the growth of tissue into the interstices of orthopedic implants and arterial grafts, as well as cuffs which anchor IV catheters in place.

Suitable biomedical poly(lactic) polymers include the poly(L-lactide), poly (D-lactide) and the poly(D-L-lactic acid). These materials are described, inter alia, on pp. 87, 88 and 115, of Baker, supra, and are biodegradable. Poly(L-lactic) acid is preferred, and those polymers having a range of molecular weights ranging from 2000 to 300.000 have been used with success.

Poly (L-lactic acid)



Poly (D-lactic acid)



The poly(lactic acid) polymers are bioerodable, and while they can be used alone, it is preferred that they be combined with either a biomedical polyurethane or a biomedical silicone.

As in the first embodiment of the invention, an additional advantage of using PLA in a polyurethane matrix is to allow improved tissue ingrowth simultaneously with a prolonged antimicrobial effect as the PLA degrades.

Thus, this embodiment of the invention is particularly important in orthopedic applications as well as in such devices as hernia patches and arterial grafts where there is a need for formation of the pseudo-intima or the growth of tissue into the interstices of orthopedic implants and arterial grafts, as well as cuffs which anchor I.V. catheters in place.

Solvents

The solvents used in preparing the coating vehicle used in the present invention includes solvents for the biomedical polymeric coating agent and/or the antimicrobial agent, and include acetic acid, methyl acetate, ethyl acetate, hexane, N-N-dimethylacetamide (DMAC), tetrahydrofuran (THF) , alcohols (e.g., alkanols), water, N-ethyl-2-pyrrolidone (NEP), n-(2-hydroxy-ethyl)-2-pyrrolidone, n-cyclohexyl-2-pyrrolidone and combinations thereof. The selection of a particular solvent or mixture of solvents will depend upon the specific biomedical polymeric coating agent being used as well as upon the particular antimicrobial agent or combination of agents.

Certain desired solvents for the polymeric coating agent may not be good solvents for an antimicrobial agent of choice. In that case, a solvent is selected which will dissolve the antimicrobial agent and will be miscible with the solvent solution of polymeric coating agent. Thus, a solvent solution of the antimicrobial agent may be combined with the biomedical polyurethane in solution in its solvent and the two solutions thereafter combined to form a uniform mixture.

Another important consideration in selecting a solvent is that the resulting solution will readily adhere to and form a film on the surface to which it is applied. Certain solvent solutions containing certain polymers do not adequately wet latex surfaces, for example, with the result that the coating is discontinuous or non-adherent.

In a preferred coating mixture where it is desired to incorporate chlorhexidine acetate with a biomedical polyurethane as coating agent, a preferred solvent is the combination of ethanol and THF, preferably in the proportions of 10% ethanol and 90% THF. Good results have been obtained where this combination contains from 1 to 25% ethanol. Another preferred combination for use with chlorhexidine acetate is NEP and THF, over a range of 1.0 to 10% NEP, more preferably 5%. Still further useful combinations of solvents include DMAC and ethyl acetate, containing from 1 to 50% DMAC, and DMAC and THF, with 1 to 25% DMAC. Each of these preferred solvent combinations results in a coating vehicle which readily wets and adheres to surfaces of medical devices fabricated from medical polyurethane, latex and/or silicone polymer, but also provides a superior adherent coating.

Antimicrobial Agents

Antimicrobial agents useful according to this first embodiment of the invention include the biguanides, especially chlorhexidine and its salts, including chlorhexidine acetate, chlorhexidine gluconate, chlorhexidine hydrochloride, and chlorhexidine sulfate, silver and its salts, including silver acetate, silver benzoate, silver carbonate, silver iodate, silver iodide, silver lactate, silver laurate, silver nitrate, silver oxide, silver palmitate, silver protein, and silver sulfadiazine, polymyxin, tetracycline, aminoglycosides, such as tobramycin and gentamicin, rifampicin, bacitracin, neomycin, chloramphenicol, miconazole, quinolones such as oxolinic acid, norfloxacin, nalidixic acid, pefloxacin, enoxacin and ciprofloxacin, penicillins such as oxacillin and pipracil, nonoxynol 9, fusidic acid, cephalosporins, and combinations thereof.

From the above list, unexpectedly, some special combinations have been found. The combination of the biguanides, especially chlorhexidine and its salts with silver salts cause a special synergistic sustaining of antimicrobial action, as described in the second embodiment of the invention below. The biguanides are also synergistically effective with nalidixic acid and its derivatives. Another effective combination is chlorhexidine acetate and pipracil.

Where the antimicrobial agent used is insoluble in the coating vehicle, as is the case with most of the silver salts and the water insoluble chlorhexidine, it is preferred that the agent be very finely subdivided, as by grinding with a mortar and pestle. A preferred product is micronized, e.g., a product wherein all particles are of a size of 5μ or less. In the case of the preferred silver sulfadiazine, a micronized product may be used.

The antimicrobial agent is preferably employed in the coating vehicle at a level such that the final coating contains from 10 to 70% by weight of the antimicrobial agent. This may be accomplished by providing a concentration of, for example, 0.5 to 3%, preferably 1%, of chlorhexidine acetate and 0.5 to 5%, preferably 1%, of silver sulfadiazine in the coating vehicle.

Unique to the invention is the use of chlorhexidine since such use internally, that is, in the human body, is heretofore unknown. Though there are examples available on the use of chlorhexidine in the bladder, such data is not relevant hereto, since it is not truly an internal use as there is no contact with the patient's circulation.

The absence of even a hint of using chlorhexidine internally is due, at least in part, to its relatively high toxicity and chemical nature (highly polar, reactive, high affinity for lipids and proteinaceous materials), leaving it a poor candidate as a systemic drug. The only way to use chlorhexidine internally is in the time release matrix system described above that allows for a dose that is non-toxic to the patient but effective against microorganisms.

Coating Vehicle

The coating vehicle is prepared according to the invention by dissolving the polymeric coating agent in a solvent therefor and by combining this solution with a solution or suspension of the antimicrobial agent. These materials can be combined at room temperature or at a slightly elevated temperature with the aid of agitation. It is preferred to employ solvents with readily evaporate from the coating at room temperature, or at an elevated temperature below that which inactivates the antimicrobial agent.

In the case of a preferred antimicrobial composition chlorhexidine acetate, either alone or in combination with silver sulfadiazine, the coating vehicle is prepared by first dissolving the polymeric coating agent such as the biomedical polyurethane in a solvent therefor, such as tetrahydrofuran (THF). The chlorhexidine is then dissolved in a solvent therefor, such as ethanol, water, or preferably N-ethyl-2-pyrrolidone (NEP), which is also miscible with THF.

Other Agents in Coating Matrix

In addition to antimicrobial agents and matrix forming materials, the coatings of the present invention may contain other compatible ingredients to advantage. For example, where anti-blood clotting activity is desired, heparin may be used, preferably at a level of 0.2%. Another useful ingredient is dextran sulfate, preferably also at a level of 0.2%

In accordance with the method of this invention, the medical device can be coated with the coating composition by known coating techniques, such as dip coating, spray coating, brush coating, roller coating, etc. Moreover, multiple coatings using the same or different polymer matrix-forming agents for each, can be used.

The coated medical device can be dried at room temperature to remove solvent or with the aid of a slightly elevated temperature over an appropriate time period.

The coating method can be repeated to build up a thicker coating on the medical device and/or to use a different antimicrobial agent in each coating, if desired.

In accordance with another preferred embodiment of the invention, the antimicrobial composition of this invention comprising a mixture of a biguanide and a silver salt in powder form is applied directly to the surface of a medical device. The method of application is one which assures adherence of the powder to the surface. One such method applies the powdered antimicrobial agent to an adhesive surface in micro layers so that minimum loss of adhesiveness occurs while imparting a high level of protection against growth of microorganisms to the surface. Other procedures include mixing the powder with adhesive prior to its application, and providing areas on the surface which alternatively contain adhesive and powdered antimicrobial agent. In one preferred method, a powder comprising a mixture of biguanide and a silver salt, most preferably a mixture of silver sulfadiazine and chlorhexidine acetate, was applied to rubber gloves at a point during their manufacture when the rubber was soft and/or semi-molten. The powder was found to adhere well after cooling of the gloves to room temperature.

It will further be understood that the invention does not require coating both the inside and outside of medical devices, especially catheters. In fact, it has been found that some catheters coated only on the outside provide necessary prophylaxis, without chemical or biological interference with the materials added to the body by the catheter. There may be instances when, for example, a coating containing an antimicrobial agent and heparin is applied only on the outside of an I.V. catheter used for providing blood to a patient. In other instances, it is advantageous to apply a coating with the anti-coagulent on the inside of the catheter to prevent clotting blockages. These specific selections are all within the scope of the invention.

Concentrations of the coating vehicle, the antimicrobial composition, the coating composition and resultant coating can be selected as desired and as illustrated by the following representative examples. In the case of the preferred combination of chlorhexidine acetate and silver sulfadiazine, good results have been obtained when the agents are present in a proportion ranging from 1:9 to 9:1, respectively. Further, it is preferred that this combination of antimicrobial agents be present at levels of from 10 to 70% by weight of the final coating.

The invention will be further illustrated by the following examples. Unless indicated otherwise, the silver sulfadiazine (AgSD) used in the examples was a micronized powder product having a particle size of 5μ or less.

It is recognized, however, that silver or its salts, including silver sulfadiazine, having a larger average particle size are useful according to this invention, and particle size selection will depend on the contemplated use of the medical device.

Example 1

A coating vehicle for use in accordance with the present invention was prepared as follows:

1 gm of chlorhexidine acetate (CHA) was added to 5 cc of N-ethyl-2-pyrrolidone (NEP). The mixture was heated to 50-60°C and agitated in a Vortex® stirrer until the CHA dissolved.

10 cc tetrahydrofuran (THF) was then added to the CHA solution in NEP and the mixture thoroughly agitated to form a uniform solution.

3 gm of Pellethane® 2363-80AE of the Dow Chemical Co. was added to 50 cc of THF. The mixture was warmed to about the boiling point of THF, 65-70°C, and stirring with a Vortex® stirrer was continued until the

polyurethane was dissolved.

1 gm of silver sulfadiazine (AgSD) powder was suspended in 35 cc of THF and vigorously agitated in a Vortex® stirrer to form a uniform suspension. The CHA solution in NEP and THF prepared above was then combined with the polyurethane solution and agitated to form a clear solution. As a last step in preparing the coating vehicle, the AgSD suspension in THF was added and the entire mixture agitated to maintain a uniform suspension. Thus was provided a coating vehicle containing 1% CHA and 1% AgSD as antimicrobial agents, together with 3% of the biomedical polyurethane. The solvent in this case was a mixture of solvents comprising 5% NEP and 95% THF. The CHA was in solution in the coating vehicle, while the AgSD was in uniform suspension.

The coating vehicle prepared above was used to coat an I.V. catheter fabricated of Pellethane® 2363-90A. The catheter was dipped in the coating vehicle while the vehicle was being continuously agitated to insure a uniform suspension. The coated catheter was then dried. A tightly adherent coating on the catheter was thus provided. A bioassay of sections of the catheter performed in accordance with the test given above with respect to Table III showed sustained activity against the microorganisms for in excess of eight days.

Example 2

Methods of Preparing I.V. and Urinary Catheters Coated with Soluble Silver Salts and Water Insoluble Chlorhexidine

In certain instances, it is necessary to use antimicrobial agents starting in solution rather than as comminuted solids. Though the invention comprises both, coating with the precursors of certain antimicrobial agents in solution has been found to be best achieved in one of two ways:

Method 1

Coating vehicle contains 1% $AgNO_3$ + 1-3% water insoluble free-base chlorhexidine + 6% polyurethane in DMAC/ethyl acetate mixture (1:1).

Water insoluble chlorhexidine is first prepared by precipitating the chlorhexidine from chlorhexidine acetate. This chlorhexidine is used for coating purposes in those instances where the chlorhexidine salts are reactive with other ingredients of the coating vehicle. For example, the acetate or gluconate salts of chlorhexidine react with silver nitrate instantly in aqueous solutions with the undesired result that each is inactivated.

Preparation of 100ml coating vehicle.

1 gm silver nitrate and 1gm water-insoluble free-base chlorhexidine were dissolved separately in 10ml portions of DMAC. 6gm polyurethane, Pellethane® 2363-80AE, were dissolved in 30ml DMAC and mixed with the silver nitrate and chlorhexidine solutions. 50ml ethyl acetate was mixed with this solution to form a coating vehicle and used for coating.

Method 2

Coating vehicle contains 0.3% $AgNO_3$ + 0.75% sulfadiazine + 1-2% chlorhexidine + 6% polyurethane in DMAC/ethyl acetate mixture (1:1).

The method of preparation of this coating solution is the same as described in Method 1 except that the sulfadiazine is added to the chlorhexidine solution and a uniform dispersion formed. The medical device (e.g., catheter) is dipped, sprayed or painted, at least once, with this solution.

A series of catheters were coated with the coating solutions prepared by methods 1 and 2 in this example and compared with a commercially available catheter coated with silver oxide. Catheters numbers 2 and 6 were prepared in accordance with method 1 above. Catheters numbers 3, 5 and 7 were prepared by method 2 above. Catheters numbers 1 and 4 were prepared in accordance with the method and using the formulation following Table I, the chlorhexidine in catheter 4 being the water insoluble type referred to in method 1 above.

The tests recorded in Table V are described elsewhere in this specification. The activity in trypticase soy broth (TSB) was determined by the bioassay described as follows:

1. Latex Urinary Catheters: 2 cm sections were soaked in 5 cc of Trypticase Soy Broth (TSB) and challenged with 10^4 CFU of a 1:1 mixture of Staph. epi and E. coli pre-diluted to 0.3 optical density at 600 nm.
2. Polyurethane I.V.: 2 cm sections soaked as above and challenged with 10^4 CFU of Staph. aureus.

The zone of inhibition determination was made following Bioassay A, described in Example 5. The Agar Lumen test was conducted as follows:

5 cc of trypticase soy agar (TSA) was solidified in a culture tube. A cork borer was used to remove a central core of agar from the tube leaving a lumen into which a 4cm section of a coated catheter having an outside dimention approximating that of the lumen opening was inserted. 1.2 cc of sterile urine was introducd into the lumen before the catheter was inserted. Once the catheter was inserted, an inoculum comprising a suspension containing $2x10^5$ CFU of a mixture of 50% Escherichia coli and 50% Staphylococcus epidermidis

was swabbed around the upper opening of the lumen adjacent the catheter.

The culture tube was incubated at 37°C. Once in each subsequent 24 hour period over the course of the test, 0.2 cc of urine was removed from within the catheter and lumen and the lumen was supplied with a fresh quantity, .2 cc, of sterile urine, which had just been inoculated with $2x10^5$ CFU of the 50% E. coli and 50% Staph. epi inoculum. At the same time, 0.01 cc of the solution removed from the lumen was tested by subculturing on a blood agar plate to determine the presence or absence of microorganisms in the liquid. In Table V below is given the number of days before growth of microorganisms was observed, either visually in the agar surrounding the lumen or in the urine samples analyzed on blood agar plates.

Comparative results between commercially coated catheters and those coated in accordance with this invention further demonstrated the significant improvement obtained; the greater the zone of inhibition, the greater the degree of suppression and cidal tendencies. Table V, below gives the results of this series of tests.

TABLE V

Antibacterial Efficacy of Urinary Catheter

Drugs in Catheter Coating	Agar Lumen Test (Days)	Zone of Inhibition (mm)	Activity in Presence of TSB (Days)
1. Silver Sulfadiazine	7 (static)	11	2
2. Silver nitrate	5 (static	9	1
3. Silver nitrate + sulfadiazine	7 (static)	11	2
4. Chlorhexidine	>15 (cidal)	20	>10
5. Silver sulfadiazine + chlorhexidine	>15 (cidal)	20	>10
6. Silver nitrate + chlorhexidine	>15 (cidal)	20	>10
7. Silver nitrate + sulfadiazine + chlorhexidine	>15 (cidal)	20	>10
8. Silver oxide (Baxter Travenol)	1 (static)	10	0
9. No drug (Control)	0	0	0

Example 3

Multicoating

At times, urinary catheters or intravenous catheters coated with biomedical polyurethane and bio-active agents or silicone (with or without PLA) and bio-active agents are found to possess surface characteristics not fully desirable. To overcome this problem, the invention further comprises the provision of a second (or more) coatings.

It has been found that a second coating applied over the biomedical polyurethane coating by spraying, dipping or otherwise, of between 0.5 and 5% of a silicone such as MDX4-4195, Dow Corning, in solution in hexane, preferably 2%, after drying, renders the coated medical device, especially a catheter, smoother in texture, with improved lubricity, without interfering with the controlled release characteristics as shown in Table VI.

TABLE VI

Retention of Antibacterial Efficacy in Presence of TSB Culture

Drug Coated Catheter Sample	Bacterial Growth Days						
	1	2	3	4	5	6	7
1	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0
3	0	0	0	0	0	1+	2+
4	0	0	0	0	0	0	0
5	0	0	0	0	1+	2+	4+
6	0	0	0	0	0	0	1+
7	0	0	0	0	0	0	1+
8	0	0	0	0	0	0	1+
9	0	0	0	0	0	0	1+
Control Catheter No Antimicrobial Agent	Heavy (++)						

2cm segments of drug coated catheters (AgSD + CHA) in a biomedical polyurethane coating agent os 3% Pellethane® 2363-80AE in a solvent of THF + ethanol or DMAC + ethylacetate were coated with a second coating by applying thereto a 2% solution of MDX4-4195 in hexane. After thorough drying to remove solvent, the segments were suspended in 5ml TSB containing 10^4 Staph. aureus and incubated at 37°C. Every 24 hours, for seven days, the bacterial growth in the culture was measured by visual turbidity and colony counts and the catheter segment was transferred to fresh culture and the experiment repeated.

Bacterial growth was properly suppressed for seven days. In addition, the catheters possessed smoother surfaces. This multi-coating process can also use PLA in the first coating, and over a range of 0.2 to 2%, preferably 1%, in the coating vehicle with improved results.

Example 4

Coating Antimicrobial Agents and Heparin or Dextran Sulfate on I.V. Catheters

It is sometimes important that certain medical devices possess bio-activity beyond antimicrobial effects. To this end, it has been found that other bio-active agents can be incorporated into the matrices without hampering the antimicrobial aspects.

As a preferred embodiment, polyurethane catheters were coated with a biomedical polyurethane coating vehicle containing 1% chlorhexidine + 1% AgSD + 0.2% heparin. The heparin imparts anti-coagulent effects to the catheter. Likewise, dextran sulfate was incorporated in the same quantities.

Table VII, below provides data showing that the addition of heparin to the coating vehicle does not interfere with antimicrobial activity of the coated device.

TABLE VII

Retention of Antibacterial Efficacy in Heparin-Coated Catheters

	Retention of Antimicrobial Activity (Days)	
	With Heparin	Without Heparin
Triple lumen catheter	6	6
Single lumen catheter	4	4

The testing was done in TSB culture as described above. The coating which was made as follows: 0.2gm of

heparin was dissolved in 2-3cc of water to which 7ml of ethyl alcohol was added. 3gm of biomedical polyurethane, Pellethane® 2363-80AE, was dissolved in 75ml of THF and the heparin solution mixed therein. 1gm of chlorhexidine acetate was dissolved in 15 ml of ethanol, after which 1gm of AgSD was suspended therein. The antimicrobial agent solution was mixed with the polyurethane solution, and agitation maintained to insure a uniform suspension. The catheters were dipped in the solution, dried and tested. Coating can also be done in stages, i.e., a first coating of antimicrobial + matrix, followed by a second of heparin + matrix.

Example 5

Arterial grafts of two commercially available types were provided with an antimicrobial coating in accordance with the invention. One was an expanded polytetrafluorethylene (PTFE) sold under the Gortex® name as a reinforced expanded PTFE vascular graft 8 mm in diameter. The second was a 6 mm straight woven Dacron® arterial graft sold by Bard.

Short sections of each of these materials were coated with each of the following coating vehicles:

1. 1% PLA + 1% polyurethane + 1% CHA + 3% pipracil in

25% NEP
75% THF

2. 0.5% PLA + 0.5% polyurethane + 1% CHA + 3% pipracil in

25% NEP
75% THF

100 ml batches of these coating vehicles were prepared by dissolving 3 gm of pipracil in 20 cc of NEP. 1 gm of CHA was separately dissolved in 5 cc of NEP. The required amount, either 1 gm or 0.5 of polyurethane was dissolved in 50 cc of THF and the same amounts of PLA were dissolved in 25 cc of THF. The four solutions were then combined and thoroughly mixed to provide the coating vehicles.

The polyurethane used was Pellethane® 2363-80AE. The PTFE sections, because of their unique structure, contain a number of cavities or interstices which require either vigorous agitation or the application of a vacuum to the section in the presence of coating vehicle to insure that the coating vehicle penetrates and permeates the graft. The woven graft requires only simple agitation in coating vehicle to provide a good coating. Both products are then air dried.

A good adherent coating formed on the Dacron® graft. In the case of the PTFE graft, its characteristic surface refused to retain a surface coating. However, the coating composition was retained in the interstices, and, on drying, retained a coating composition having, by weight, one part biomedical polyurethane, one part PLA, one part CHA, and three parts pipracil in the case of coating 1, and .5 parts each of PLA and polyurethane, with one part CHA and three parts pipracil for coating 2.

The activity of the processed grafts are determined by the two types of bioassays described below:

Bioassay A

- 2cm sections of graft are embedded in a 5% sheeps blood agar plate which was inoculated with $2x10^4$ CFU Staph. aureus. Activity was determined by measuring the zone of inhibition. The graft sections were transferred to newly inoculated plates daily until antibacterial activity ceased.

Bioassay B

- 1cm section of graft were soaked in 5cc of trypticase soy broth (TSB) which was inoculated with 10^4 CFU of Staph. aureus. If there was no turbidity after 24 hours incubation at 37° C, then the material was deemed to be bacteriostatic. The grafts were transferred to new TSB and inoculated daily.

Bioassay A Group	Results Zone of Inhibition (mm)			
Days	1	3	6	9
PTFE (Formula 1)	23	19	16	12
PTFE (Formula 2)	29	20	16	12
Bard (Formula 1)	29	15	12	12
Bard (Formula 2)	29	15	14	11.5
Untreated Control	0			

Bioassay B

All processed groups show activity for more than 10 days.

Untreated Control showed heavy growth and turbidity after one day.

Example 6

An expanded polytetrafluorethylene (PTFE) hernia path was impregnated with an infection-resistant material comprising silver sulfadiazine and chlorhexidine acetate in a biodegradable matrix of poly(lactic acid) using the following method.

An impregnating vehicle was prepared by mixing 0.5% chlorhexidine acetate, 0.5% silver sulfadiazine and 1% poly(lactic acid), mw 44,000, in a solvent mixture comprising 95% ethanol and THF in the proportions of 10:90. The chlorhexidine acetate and PLA are in solution in this mixture; the silver sulfadiazine is in suspension.

An expanded PTFE hernia path, 2x2 cm and having a thickness of about 0.5 cm was soaked for 5 minutes in the impregnating vehicle prepared above, with continuous stirring to maintain a uniform suspension. The patch was then removed from the suspension, air dried for about one minute and then placed in an oven at 40° C for 24 hours.

The antibacterial efficacy of the patch was evaluated, utilizing Bioassay B described in Example 5 above. Several 1 cm^2 pieces were cut and soaked in TSB and kept in water bath shakers at 37° C. The TSB is changed daily and 4 pieces were removed at different intervals and tested for zone of inhibition. The results are given in the following table:

Days of Soaking	Zone of Inhibition (mm) against Staph. aureus after 1 day
0	24
1	22
3	20
6	20

Example 7

Method of in situ Incorporation of Silver Sulfadiazine and Chlorhexidine in Hernia Patch

The interstices of a hernia patch, which is made up of expanded PTFE, are too small for a sufficient amount of silver sulfadiazine (AgSD) molecules to enter. Therefore, silver sulfadiazine is precipitated in situ by treating the patch with sodium sulfadiazine (NaSD) and silver nitrate. The following methods were used to incorporate silver sulfadiazine and chlorhexidine acetate (CHA) into the interstices of a patch.

1. An expanded polytetrafluorethylene (PTFE) hernia patch, 2x2 cm and having a thickness of about 0.5 cm is first soaked in:

   (a) a 95% ethanol solution of 0.5% silver sulfadiazine and 0.5% chlorhexidine acetate for 2-3 minutes, removed, dried for about one minute;

   (b) the patch is then soaked in 0.25% $AgNO_3$ solution for 2-3 minutes, removed and air dried. The patch is then placed in an oven at 40° C for 24 hours.

2. The procedure is the same as in 1, but the first solution contains 0.4% sodium sulfadiazine, 0.5% chlorhexidine acetate, and 1% PLA, mw 44,000, in a solvent comprising a 95% ethanol:THF mixture (10:90). In an alternative to both the 1 and 2 methods, the first dipping step was done in $AgNO_3$ solution

and then in the mixture of sodium sulfadiazine and chlorhexidine acetate.

Evaluation of Antibacterial Efficacy of Patches Coated by this Process

Following the bioassay method of Example 6, several 1 cm^2 pieces were cut and soaked in TSB and kept in water bath shakers. The TSB was changed daily and 4 pieces were removed at different intervals and tested for zone of inhibition.

Coating Procedure	Zone of Inhibition (Days)		
	1	3	6
Method A			
NaSD + CHA → $AgNO_3$	23	21	20
$AgNO_3$ → NaSD + CHA	22	21	20
Method B			
NaSD + CHA + PLA → $AgNO_3$	22	20	19
$AgNO_3$ → NaSD + CHA + PLA	22	20	19

Example 8

A coating vehicle for use in accordance with the present invention was prepared as follows:

1 gm of chlorhexidine acetate (CHA) was added to 5 cc of N-ethyl-2-pyrrolidone (NEP). The mixture was heated to 50-60°C and agitated in a Vortex® stirrer until the CHA dissolved.

10 cc tetrahydrofuran (THF) was then added to the CHA solution in NEP and the mixture thoroughly agitated to form a uniform solution.

3 gm of Pellethane® 2363-80AE of the Dow Chemical Co. was added to 50 cc of THF. The mixture was warmed to about the boiling point of THF, 65-70°C, and stirring with a Vortex® stirrer was continued until the polyurethane was dissolved.

1 gm of silver sulfadiazine (AgSD) micronized powder was suspended in 35 cc of THF and vigorously agitated in a Vortex® stirrer to form a uniform suspension. The CHA solution in NEP and THF prepared above was then combined with the polyurethane solution and agitated to form a clear solution. As a last step in preparing the coating vehicle, the AgSD suspension in THF was added and the entire mixture agitated to maintain a uniform suspension. Thus was provided a coating vehicle containing 1% CHA and 1% AgSD as antimicrobial agents, together with 3% of the biomedical polyurethane. The solvent in this case was a mixture of solvents comprising 5% NEP and 95% THF. The CHA was in solution in the coating vehicle, while the AgSD was in uniform suspension.

The coating vehicle prepared above was used to coat an I.V. catheter fabricated of Pellethane® 2363-90A. The catheter was dipped in the coating vehicle while the vehicle was being continuously agitated to insure a uniform suspension. The coated catheter was then dried. A tightly adherent coating on the catheter was thus provided.

Example 9

Synergism of Silver Sulfadiazine (AgSD) and Chlorhexidine (CHA)

The results of experiments described below indicate that coating silver salts, preferably sulfadiazine, and chlorhexidine or its salts onto medical devices imparts prolonged antibacterial activity. In addition, in vitro studies show that chlorhexidine exhibits a synergistic effect when combined with silver sulfadiazine and thus increases the antimicrobial spectrum. AgSD + CHA also kills 99.9% of the bacterial population faster than

chlorhexidine alone which is important for its use in medical gloves and condoms. Furthermore, when wound dressings (Epilock® dressings) coated with silver sulfadiazine and chlorhexidine were tested for zone of inhibition against a mixed culture of Staph. aureus and Ps. areuginosa, a synergistic effect was observed.

Analytical Procedures for Determinating the Drug Content and Rate of Release from Devices

Determination of silver (Ag), sulfadiazine (SD) and chlorhexidine acetate (CHA) values is performed as follows:

Silver and SD

The devices (catheters) were coated with radioactive silver sulfadiazine (^{110}AgSD) and after measuring the initial radioactivity they were suspended in culture media or saline. The catheters were transferred daily to fresh media or saline and the radioactivity remaining in the catheter segments were measured using a Nuclear Chicago 1185 automated gamma counter. The amount of SD released was measured by determining the SD content of the media using a calorimetric method (Bratton-Marshal Test).

Initial levels of SD in the catheters were determined by extracting the SD from the catheters with 0.2 molar nitric acid.

CHA

CHA levels are determined spectrophotometrically (231nm and 254nm) using a Hitachi® 2000 double beam UV/VIS system. Initial levels were measured by extracting the CHA from the catheter using warm ethanol. The CHA released into the media was also measured spectrophotometrically. These spectrophotometric levels wer corroborated by bioassay such as zone of inhibition tests.

In vitro Studies

Different concentrations of silver sulfadiazine or chlorhexidine alone or in combinations were added to mixed cultures of Ps. areuginosa and Staph. aureus (10^5 CFU each organism) in 2 ml trypticase soy broth (TSB) and incubated along with control cultures. 0.1 ml aliquots were removed from these cultures and diluted to 10 ml (1 to 100 dilution) at 10 minutes, 20 minutes and 40 minutes. 0.2 ml of these diluted samples were subcultured on blood agar plates and colony counts were made 24 hours post incubation. The results are given the following Table VIII.

TABLE VIII

Bacterial Inhibition

Antimicrobial Agent	Concentration (µmole/2 ml)	Colony Forming Units (CFU)		
		10 minute	20 minute	40 minute
None	0	$>10^6$ (S&P)	$>10^6$ (S&P)	$>10^6$ (S&P)
AgSD	1.0	$2x10^5$ (S&P)	$1x1x10^5$ (S&P)	$1.2x10^5$ (S&P)
CHA	1.0	$1x10^3$ (S)	0	0
AgSD + CHA	1.0 + 1.0	0	0	0
AgSD	0.5	$>10^6$ (S&P)	$>10^6$ (S&P)	$>10^6$ (S&P)

CHA	0.5	$1x10^5$ (S)	$3.7x10^4$ (S)	$2x10^2$ (S)
AgSD + CHA	0.5 + 0.5	0	0	0

S&P = Staph. aureus and Ps. areuginosa
S = Staph. aureus

The results show:

1. chlorhexidine acts rapidly, and by 20 minutes kills the organisms present;
2. silver sulfadiazine exhibits steady and prolonged suppression of growth (also see the example relating to wound dressings below); and
3. AgSD + CHA demonstrate a marked improvement over the individual results as there is even a more rapid kill (10 minutes), and prolonged suppression.

The results clearly show a fast and prolonged and synergistic antibacterial activity for the combination of AgSD + CHA, exhibiting far superior results than by using each such antimicrobial agent alone.

Example 10

Synergistic results are also found when other silver salts are combined with chlorhexidine, as shown in Table IX, below.

TABLE IX

Synergistic Effect of Silver Compounds and Chlorhexidine against Staph. aureus, in vitro

Drug Concentration in Culture	Colony Count (Minutes)	
	20	60
100µg silver sulfadiazine	9,500	8,000
100µg silver oxide	7,500	8,000
100µg silver carbonate	9,200	6,000
100µg chlorhexidine acetate	6,250	4,000
50µg silver sulfadiazine + 50µg chlorhexidine acetate	4,800	0
50µg silver oxide + 50µg chlorhexidine acetate	3,700	0
50µg silver carbonate + 50µg chlorhexidine acetate	4,300	0
100µg silver nitrate	10,500	11,000
100µg chlorhexidine, water insoluble	6,000	3,000
50µg silver nitrate + 50µg chlorhexidine, water insoluble	100	0
CONTROL	16,000	15,000

For Table IX, 3 ml of TSB culture of Staph. aureus (10^4 CFU/ml) containing the drug were incubated for one hour at 37°C and the colony counts measured. The results achieved further show the synergistic interaction between silver salts and chlorhexidine salts in causing complete suppression of growth by 60 minutes, whereas each anti-bacterial agent, alone, showed only partial suppression.

Example 11

Methods for the Preparation of Coated Medical Devices and Evaluation of Antibacterial Activity

Certain medical devices are comprised of materials not fully compatible with biomedical polyurethane as a coating vehicle, requiring, for compatible matrices, the use of a biomedical silicone, with or without a biodegradable polymer such as poly(lactic acid) (PLA).

Method A

Chlorhexidine diacetate is mixed uniformly in 1% to 10%, preferably 5%, silicone solution in ethyl acetate, or silicone solution containing .2 to 2%, preferably 0.5% or 1% poly(lactic acid), molecular weight 2000. The medical device is dipped for 10 seconds in this suspension which is kept at room temperature. The silicone used was Silastic® Medical Adhesive Silicone Type A.

Method B

0.5 to 10% chlorhexidine diacetate is mixed uniformly in 1% PLA solution (equal amounts of 2,000, 44,000, 100,000 and 300,000 molecular weight PLA) in ethyl acetate. This antimicrobial suspension is kept at 50°C in a water bath and mixed continuously. The medical device to be coated is dipped for one minute in this suspension, removed and dried.

In both of the above methods, other antimicrobial agents can also be used either singly or in combination as shown below.

Coating of Latex Gloves

The fingers of latex medical gloves were washed, dried and dip-coated with (a) chlorhexidine acetate (CHA), (b) CHA and silver sulfadiazine (AgSD), and (c) AgSD using antimicrobial suspensions prepared by Method A above. The silicone used in this test was a mixture of equal parts by weight of Silastic® Medical Adhesive Silicone Type A, and MX-4-4159, a fluid comprising equal parts of an active polydimethyl siloxane and a solvent therefor comprising mixed aliphatic and isopropanol solvents. The PLA employed was a poly(L-lactic acid) procured from Polysciences, Inc., Warington, Pennsylvania, having various molecular weights. PLA-2000 has a molecular weight of 2000. The suspension had the following composition:

1. 10% CHA + 10% silicone + 0.5% PLA-2000
2. 5% CHA + 5% AgSD + 10% silicone + 0.5% PLA-2000
3. 10% silver sulfadiazine + 10% silicone + 0.5% PLA-2000

The antibacterial efficacy was tested against a mixed culture of Pseudomonas aeruginosa and Staphylococcus aureus having 10^4 CFU of each per 2 ml of culture.

The coated fingers were suspended in culture tubes and 2 ml of 5% bovine albumin solution containing the mixed bacterial culture were added to it and incubated at 37°C. The rate of killing was determined by taking aliquots at 10, 20 and 40 minutes and subculturing on blood agar plates for colony counts. The results are given in Table X below.

TABLE X

Colony Counts of Staph. aureus and Ps. aeruginosa (Colony Forming Units - CFU/2 ml Culture)

Antimicrobial Agent on Gloves	10 Minutes		20 Minutes		40 Minutes	
	Staph. aureus	Ps. aer.	Staph. aureus	Ps. aer.	Staph. aureus	Ps. aer.
CHA	$8x10^3$	0	$2x10^3$	0	0	0
CHA + AgSD	$4x10^3$	0	0	0	0	0
AgSD $5x10^3$	$1x10^4$	$1.2x10^4$	$5x10^3$	$8x10^3$	$4x10^3$	
None (Control)		$1x10^4$	$1x10^4$	$1x10^4$	$8x10^3$	
$2x10^4$ $8x10^3$						

These results demonstrate improved and sustained suppression of bacterial growth when using the combination of CHA + AgSD on gloves.

Example 12

Coating of Urinary Catheters and Evaluation of Antibacterial Activity

Using the methods described in A and B in Example 11 above, latex urinary catheters were coated with a coating vehicle containing Silastic® Medical Adhesive Silicone Type A in Method A and PLA in Method B, both having various amounts of chlorhexidine and/or silver sulfadiazine and 2.0 cm segments were soaked in either 5 ml trypticase soy broth (TSB or 5 ml urine inoculated with a mixture of 10^4 organisms of Staph. epi and E. coli. After 24 hours of incubation at 37°C, the media was subcultured to quantitatively determine bacterial levels. The segments were then transferred to fresh media which was re-inoculated. This procedure was continued until the urinary catheter segments no longer presented antibacterial activity. The results, showing significant retention of bio-active material are given in Table XI below.

TABLE XI

Retention of Antibacterial Activity of Coated Urinary Catheters

Antimicrobial Agent on Urinary Catheters	Retention (Days)			
	% Anti-Microbial in coating Solution	In Presence of Urine	In Presence of TSB	Nutrient Agar Plate
Method A - CHA	10	5	4	>7
Method A - CHA	5	4	3	5
Method A - AgSD	5	2	2	5
Method A - CHA + AgSD	5+5	3	3	>7
Method A - None (Control)	0	0	0	0
Method B - CHA	10	6	4	>7
Method B - CHA	5	4	3	5
Method B - AgSD	4	2	2	5
Method B - CHA + AgSD	5+5	3	3	6
Method B - None (Control)	0	0	0	0

CHA = chlorhexidine acetate

AgSD = silver sulfadiazine

Example 13

Antibacterial Efficacy of Coatings Containing Chlorhexidine Acetate and Biodegradable Polymers on Polyurethane I.V. Catheters

Using the method described as Method B in Example 11 above, I.V. catheters fabricated of Pellethane® 2363-80AE, a biomedical polyurethane, were coated with a coating vehicle which, in a first series, contained 1% chlorhexidine acetate in a solvent comprising 10% of 95% ethanol and 90% ethyl acetate. A second series used a coating vehicle containing 1% chlorhexidine acetate and 3% of Pellethane® 2363-80AE in a solvent comprising 10% of 95% ethanol and 90% of THF. The third series used a coating vehicle comprising 1% chlorhexidine acetate, 5% of Silastic® Type A Medical Adhesive, a polymethyl siloxane, and 2% of MDX 4-4159, a silicone comprising 50% of an amino functional polydimethyl siloxane copolymer and 50% mixed aliphatic and isopropanol solvents. In addition, each of the three series contained a biodegradable polymer at a level of 1%; the polymers were obtained from Polyscience.

The procedure described in Example 12 was used to test 2.0 cm segments of the coated catheter. The results obtained are summarized in the following table:

Biodegradable Polymers	1-day Zone of Inhibition (mm)		
	CHA Alone	CHA with Polyurethane	CHA with Silicone
Poly(lactic acid), mw 100,000	21	21	20
Polycaprolactone	20	19	19
Polyhydroxybutyric acid, mw 30,000	20	21	21

The zone of inhibition was tested on blood agar culture plates seeded with Staph. aureus (10^4 organisms).

Example 14

Multicoating

At times, urinary catheters or intravenous catheters coated with biomedical polyurethane and bio-active agents or silicone (with or without PLA) and bio-active agents are found to possess surface characteristics not fully desirable. To overcome this problem, the invention further comprises the provision of a second (or more) coatings.

It has been found that a second coating applied over the biomedical polyurethane coating by spraying, dipping or otherwise, of between 0.5 to 5% of a silicone fluid such as the MDX4-4159 described in Example 11 in solution in hexane, preferably 2%, after drying, renders the coated medical device, especially a catheter, smoother in texture, with improved lubricity and improved retention characteristics, as shown in Table XII.

TABLE XII

Retention of Antibacterial Efficacy in Presence of TSB Culture

Drug Coated Catheter Sample	Bacterial Growth Days						
	1	2	3	4	5	6	7
MDX Coating							
1	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0
3	0	0	0	0	0	1+	2+
4	0	0	0	0	0	0	0
5	0	0	0	0	1+	2+	4+
6	0	0	0	0	0	0	1+
7	0	0	0	0	0	0	1+
8	0	0	0	0	0	0	1+
9	0	0	0	0	0	0	1+
No MDX Coating							
1	0	0	0	0	0	1+	
2	0	0	0	0	1+	1+	
3	0	0	0	0	1+	1+	
4	0	0	0	0	1+	1+	
5	0	0	0	0	1+	1+	
6	0	0	0	0	0	1+	
Control Catheter No Antimicrobial Agent			Heavy (++)				

2 cm segments of drug coated catheters (AgSD + CHA) in a biomedical polyurethane coating agent of 3% Pellethane® 2363-80AE in a solvent of THF + ethanol or DMAC + ethylacetate were coated with a second coating by applying hereto a 2% solution of MDX4-4159 in hexane. After thorough drying to remove solvent, the segments were suspended in 5 ml TSB containing 10^4 Staph. aureus and incubated at 37°C. Every 24 hours, for seven days, the bacterial growth in the culture was measured by visual turbidity and colony counts and the catheter segment was transferred to fresh culture and the experiment repeated.

Bacterial growth was properly suppressed for seven days. In addition, the catheters possessed smoother surfaces. This multicoating process can also use PLA in the first coating, and over a range of 0.2 to 2%, preferably 1%, in the coating vehicle with improved results.

Example 15

Coating Antimicrobial Agents and Heparin or Dextran Sulfate on I.V. Catheters

It is sometimes important that certain medical devices possess bio-activity beyond antimicrobial effects. To this end, it has been found that other bio-active agents can be incorporated into the matrices without hampering the antimicrobial aspects.

As a preferred embodiment, polyurethane catheters were coated with a biomedical polyurethane coating vehicle containing 1% chlorhexidine + 1% AgSD + 0.2% heparin. The heparin imparts anti-coagulent effects to the catheter. Likewise, dextran sulfate was incorporated in the same quantities.

Table XIII, below provides data showing that the addition of heparin to the coating vehicle does not interfere with antimicrobial activity of the coated device.

TABLE XIII

Retention of Antibacterial Efficacy in Heparin-Coated Catheters

	Retention of Antimicrobial Activity (Days)	
	With Heparin	Without Heparin
Triple lumen catheter	6	6
Single lumen catheter	4	4

The testing was done in TSB culture as described above. The coating which was made as follows: 0.2 gm of heparin was dissolved in 2-3 cc of water to which 7 ml of ethyl alcohol was added. 3 gm of biomedical polyurethane, Pellethane® 2363-80AE, was dissolved in 75 ml of THF and the heparin solution mixed therein. 1 gm of chlorhexidine acetate was dissolved in 15 ml of ethanol, after which 1 gm of AgSD was suspended therein. The antimicrobial agent solution was mixed with the polyurethane solution, and agitation maintained to insure a uniform suspension. The catheters were dipped in the solution, dried and tested. Coating can also be done in stages, i.e., a first coating of antimicrobial + matrix, followed by a second of heparin + matrix.

Example 16

Coating of Wound Dressings

Johnson and Johnson gauze dressings and Epilock® dressings manufactured by Dermalock Medical Corporation were coated with antimicrobial agents. These coated dressings were prepared using methods (a) and (b) above. The zone of inhibition was tested against a mixture of Ps. aeruginosa and Staph. aureus cultures on nutrient agar plate.

TABLE XIV-A

Antibacterial Activity of Johnson and Johnson Dressings

Antimicrobial Agent in Dressings	% Antimicrobial Agent in Coating Solution	Zone of Inhibition (mm)	
		1 day	2 day
Method A - CHA	10	27	20
Method A - AgSD	5	25	18
Method A - CHA + AgSD	5+5	25	20
None (Control)	0	0	0

TABLE XIV-B

Antibacterial Activity of Epilock® Dressings

Antimicrobial Agent in Dressings	% Antimicrobial Agent in Coating Solution	Zone of Inhibition (mm)				
		1	2	3	4	5 Days
Method A - CHA	10	28	28	43	40	25
Method A - AgSD	5	30	35	43	27	28
Method A - CHA + AgSD	5+5	34	45	43	27	34
Method B - CHA	10	27	21	22	24	24
Method B - AgSD	5	31	35	35	0	0
Method B - CHA + AgSD	5+5	38	28	37	30	25
None (Control)	0	0	0	0	0	0

These results demonstrate the improvement in using the synergistic combination, as well as the general efficacy of the process. Wound dressings may also be provided with an adhesive on one side (to attach to the wound). In such cases, the invention further comprises seven methods of application of the antimicrobial agent:

1. Suspending the antimicrobial agents, preferably silver sulfadiazine and chlorhexidine in the quantities of 1-5% total, in a carrier that evaporates but does not solubilize the adhesive, instead leaving the adhesive intact, e.g., an alcohol, and spraying the agent-containing carrier upon the dressing, or dipping the dressing into the agent-containing carrier solution.
2. Placing the antimicrobial agents in a solution containing silicone or polyurethane (preferably 1%) and a carrier (preferably ethyl acetate, THF or H_2O and spraying it upon the dressing, or dipping the dressing into it.
3. Applying powdered antimicrobial agents (preferably silver sulfadiazine and chlorhexidine) to the adhesive in microlayers that do not eliminate adhesion.
4. Admixing powdered antimicrobial agents with adhesive prior to application.
5. Adding a biodegradable material containing antimicrobial agents to the adhesive to provide controlled-release through degradation.
6. Providing spots containing antimicrobial agents, surrounded by adhesive.
7. Providing a biodegradable or nonbiodegradable adhesive composition containing antimicrobial agents.

Example 17

Method of Coating Antimicrobial Agents on the Surface of Latex Gloves During Automated Manufacturing Process

The invention is especially useful in the automated manufacturing of gloves. There are two methods found useful in the coating of the combination of chlorhexidine and silver sulfadiazine.

Method 1

Latex gloves are typically manufactured by (1) dipping a form in molten latex, (2) removing the latex form and transferring it to a dryer, (3) removing the form with attached glove from the dryer and immediately spraying it with a dusting powder, as it cools. A suspension of silver sulfadiazine in alcohol or water in an aqueous silicone latex emulsion (1-5% by volume) + chlorhexidine (1-5% + dusting powder (2-10%) is sprayed on the gloves as the gloves are dispenesed from the dryer at 120°C. At this temperature, the antimicrobial agents and the

dusting powder particles adhere well to the soft and/or semi-molten surfaces of the gloves. The antimicrobial activity is not in any way altered as a consequence of this process, because of the falling temperature of the gloves, as they cool. This is a preferred procedure in cases where presence of other organic solvents in the coating process is a concern to the manufacturer.

Method 2

Sterile corn starch-based dusting powder is admixed with silver sulfadiazine (1-5% by weight) and chlorhexidine (1-5% by weight) in powdered form, and the mixture is sprayed on the gloves as they are dispensed from the dryer at 120° C, and start to cool. The dusting powder with enhanced antimicrobial activity remains with the gloves.

Example 18

Preparation of Infection-Resistant Devices with Silver Sulfadiazine and Chlorhexidine Using a Mixture of Silicones as the Polymeric Coating Agent

In order to obtain a coating which is lubricious, adheres well to the catheter and also releases the drug in a controlled dosing manner, a mixture of Silastic® Medical Adhesive Type A, a polydimethyl siloxane, and MDX-4-4159, a fluid silicone comprising equal parts of an amino functional Polydimethyl siloxane copolymer and a mixed aliphatic and isopropanol solvent were used as the polymericcoating agents. Silastic® Medical Adhesive Silicone Type A alone forms an undesirable surface, while the MDX-4-4159 alone does not form an adherent film on the surface. However, use of a mixture of these two silicones in 1:1 proportions gives a coating vehicle which forms a film with the desired biocompatible characteristics. The Silastic® functions as the bonding agent whereas the MDX-4-4159 imparts lubricity to the surface. In addition, the MDX-4-4159 prolongs the release of the antimicrobial agent.

The coating agent was prepared by dispersing 2.5ml of Silastic® Medical Adhesive Type A in 55ml of THF to which 2.5 ml of MDX-4-4159 is added. 4 g of Ag SD are suspended in 30ml and 2g of CHA are dissolved in 10ml of ethanol. The AgSD suspension is mixed with the silicone dispersons and finally the CHA solution is added dropwise while the preparation is agitated. Either 5% NEP or 5% DMAC can be substituted for ethanol in the above formulation.

The coating agent prepared above was used to apply a coating on catheters fabricated from silicone, polyurethane and latex substrates. The coatings were applied by dipping and drying, as described in Example 2. Results are given in Table XV below.

TABLE XV

Antibacterial Efficacy of Polyurethane I.V. Catheters and Latex or Silicone Urinary Catheters Coated with A silicone Matrix

Catheter Type	Drug in Catheter	Days of Activity*
Polyurethane I.V.	CHA	2
Polyurethane I.V.	AgSD + CHA	4
Latex urinary	AgSD	2
Latex urinary	AgSD + CHA	4
Silicone urinary	AgSD	3
Silicone urinary	AgSD + CHA	4

* Determined via Bioassay A. Inoculum used to assay urinary catheter is a 10^4 CFU of a 1:1 mixture of Staph. epi and E. coli; 10^4 CFU of Staph. aureus is used to challenge the I.V. catheter.

Example 19

Silver sulfadiazine and chlorhexidine acetate were added over a range of proportions to cultures of Staph.

aureus containing 10^5 colony forming units (CFU) in 2 ml trypticase soy broth (TSB) and the cultures were incubated along with control cultures at 37° C. 0.1 ml aliquots were removed from these cultures and diluted to 10 ml, a 1:100 dilution after one hour. 0.2 ml of these diluted samples were subcultured on blood agar plates and colony counts were made 24 hours post incubation. The results are given in the following Table XVI.

TABLE XVI

Synergism of Different Combinations of Silver Sulfadiazine (AgSD) and Chlorhexidine (CHA) against Staph. aureus

Concentration µg/2 ml AgSD + CHA		Bacterial Inhibition Colony Forming Units After 1 Hour
0	100µg	650
25µg	75µg	100
50µg	50µg	150
75µg	25µg	100
87.5µg	12.5µg	150
100µg	0	3,100
0	0	4,100

Example 20

Coating of Latex Gloves

The fingers of latex gloves were washed and dried. They were then sprayed with a fine mist spray of a coating solution to provide a uniform coating of solution on the glove surface, sufficient to provide complete wetting thereof without runoff. The coating solutions were prepared by dissolving 1% Silastic® Medical Adhesive Type A and 1% of the silicone MDX4-4159 in ethyl acetate, followed by dissolving and dispersing the chlorhexidine acetate and silver sulfadiazine, respectively, therein. The coating was air dried for 24 hours and the gloves tested using the following test:

Treated glove fingers were draped over the tops of culture tubes with the treated side with sprayed on coating forming the inside on the cup shape. Then 3.0 ml of TSB containing 10^4 colony forming units of Staph. aureus was dispensed in each finger and all placed in a water bath shaker at 37° C. Samples were removed at 15 minutes, 1 hour, 2 hours, and 4 hours, diluted 1-10, and the solution placed on blood agar in 2.0 ml amounts.

The results of the test are summarized in the following Table XVII.

TABLE XVII

Antibacterial Efficacy of Drug Coated Gloves against Staph. aureus

Drug in Coating Solution	15 Minutes	1 Hour	2 Hours	4 Hours
None (Control)	12,000	15,000	20,000	50,000
Chlorhexidine (1%)	100	0	0	0
Silver Sulfadiazine (2%)	3,300	200	0	0
Silver Sulfadiazine (1%) + Chlorhexidine (1%)	0	0	0	0

It is noted that the gloves coated according to this procedure were flexible and met all other requirements for high quality latex gloves.

Example 21

The fingers of latex gloves were washed, dried, and sprayed with a fine mist of a coating solution to provide a uniform coating of solution on the glove surface, sufficient to provide a complete wetting thereof without runoff. The coating solutions were prepared by dissolving 1% Silastic® Medical Adhesive Type A and 1% of the silicone MDX4-4159 in ethyl acetate, followed by dissolving or dispersing the chlorhexidine acetate and silver sulfadiazine respectively therein. The coating was air dried for 24 hours and the gloves tested using the following test:

Treated glove fingers were draped over the tops of culture tubes with the treated side with sprayed on coating forming the inside on the cup shape. Then 3.0 ml of TSB containing 10^3 colony forming units of Candida albicans was dispensed in each finger and all placed in a water bath shaker at 37° C. Samples were removed at 15 minutes, 1 hour, 2 hours, and 4 hours. They were diluted 1-10 and plated on blood agar in 2.0 ml amounts.

The results of the test are summarized in the following Table XVIII.

TABLE XVIII

Antibacterial Efficacy of Drug Coated Gloves against Candida albicans

Drug in Coating Solution	Colony Counts in Culture			
	15 min.	1 hour	2 hours	4 hours
None (Control)	1,400	2,000	4,000	6,000
Chlorhexidine (1%)	75	0	0	0
Silver sulfadiazine (2%)	1,650	1,500	1,500	2,200
Silver sulfadiazine (1%) + Chlorhexidine (1%)	0	0	0	0

As in Example 20, the gloves coated according to this procedure were flexible and met all requirements for high quality latex gloves.

Example 22

The fingers of latex gloves were washed and dried. They were then sprayed with a fine mist spray of the

coating solution in runs 1-3 below to provide a uniform coating of solution on the glove surface, sufficient to provide a complete wetting without runoff, after which the gloves were dried for 24 hours. In run 4, the powder was blown on to the gloves to form a uniform coating.

The coating solutions were prepared having the following ingredients:

1. 1% MDX4-4159 + 1% Silastic® Medical Adhesive Type A + 1% CHA + 1% AgSD + 2% starch-based dusting powder in ethyl acetate.
2. 1% CHA + 1% AgSD + 2% dusting powder in ethanol.
3. 1% chlorhexidiene gluconate (CHG) + 1% AgSD + 2% dusting powder in ethanol.
4. A mixture of CHA + AgSD + dusting powder in equal weight ratios.

The coated gloves were tested, following the procedure set forth in Example 16 above. The results are given in Table XIX.

TABLE XIX

Antibacterial Efficacy of Drug Coated Gloves against Staph. aureus

Coating Solution	Colony Counts in Culture	
	15 min.	1 hour
1	0	0
2	0	0
3	0	0
4	0	0
None (Control)	12,000	15,000

It is noted that other medical gloves, including surgical and examination gloves, fabricated from other materials such as polyurethane, polyethylene, polypropylene, and polyvinyl acetate, may be coated following the process of this invention.

It is further noted that in both the dry powder process and the so-called wet powder process using a vehicle such as ethanol, the antimicrobial powders and dusting powders may be applied separately, and in any sequence.

Example 23

This example illustrates the coating of medical gloves with a coating composition containing an aqueous silicone emulsion.

15 grams of starch-based dusting powder is suspended in 50 ml of deionized water. The suspension is then mixed with 44.5 ml of deionized water in which 2 grams of micronized silver sulfadiazine is suspended. To this mixture is added .5 cc of L.E. 46, a silicone emulsion containing 35% dimethyl siloxane, sold by Dow Corning Company. Finally, 5 cc of a 20% chlorhexidine gluconate in water is added and the mixture stirred to maintain a uniform suspension.

Washed latex glove fingers are dipped into the mixture and air dried for one minute to provide an adherent, infection-resistant, coating.

Example 24

Latex urinary catheters were provided with coatings including a series of antimicrobial agents. A coating solution was prepared containing 6% Dow Pellethane® 80AE in solvent comprising 5% NEP and 95% THF. The catheters were dipped in the solution to provide a uniform coating, and dried for 24 hours to remove the solvent. When used alone, the Ag salt was used at a 5% level. When a combination of agents were used, the silver salt was at a 2% level, as was the CHA. All silver salts were very finely divided, either by grinding in a mortar and pestle, or by purchase of micronized grade materials. Three 1 cm segments of each catheter were placed in the center of blood agar plates seeded with 10^4 CFU of a 1:1 mixture of Staph. epi and E. coli, one section to each plate, and the zone of inhibition was measured after incubation at 37°C for 24 hours. The results are given in the following Table XX.

TABLE XX

Antibacterial Efficacy of Drug Coated Urinary Catheters against Staph. epi and E. coli

Drug on Catheter	Zone of Inhibition (mm), Days					
	Days 1	2	3	4	5	6
Chlorhexidine (CHA)	18	23	15	16	15	14
Silver acetate	12	13	12	12	12	11
Silver acetate + CHA	20	21	14	14	12	12
Silver benzoate	13	12	10	11	11	12
Silver benzoate + CHA	18	20	12	13	13	14
Silver carbonate	13	12	12	12	12	13
Silver carbonate + CHA	20	23	19	12	13	13
Silver iodate	10	0	0	0	0	0
Silver iodate + CHA	18	20	15	14	14	15
Silver laurate + CHA	22	24	19	18	18	17
Silver protein	10	0	0	0	0	0
Silver protein + CHA	26	26	15	16	16	17
Silver palmitate + CHA	26	26	23	18	18	18
Silver chloride	11	6	6	10	10	10
Silver chloride + CHA	20	15	14	15	15	15
Silver oxide	14	12	11	12	12	12
Silver oxide + CHA	22	25	15	14	15	15
Silver sulfadiazine	8	8	7	10	10	10
Silver sulfadiazine + CHA	20	15	15	15	16	16
Silver tannate + CHA	20	-*	-	-	-	-

* Experiment discontinued after 1 day because of poor quality coating.

Example 25

I.V. catheters fabricated of Pellethane® 2363-90A were provided with coatings including a series of antimicrobial agents. A coating solution was prepared containing 6% Dow Pellethane® 2363-80AE and the drug in a solvent comprising 5% N-ethyl-2-pyrrolidone (NEP) and 95% tetrahydrofuran (THF). When used alone, the Ag salt was used at a level of 5%. When combined with CHA, each was used at a level of 2%. The catheters were dipped in the solution to provide a uniform coating on the device, and thereafter allowed to dry for 24 hours to remove the solvent.

Three 1 cm segments of each catheter were placed in the center of blood agar plates seeded with 10^4 CFU of Staph. aureus, one section to a plate, and the zone of inhibition was measured after 24 hours at 37°C.

Results, expressed as the average of 3 determinations, are given in the following Table XXI.

TABLE XXI

Antibacterial Efficacy of Drug Coated I.V. Catheters against Staph. aureus

Drug on Catheter	Zone of Inhibition (mm),				
	1	2	3	4	5
Chlorhexidine (CHA)	15	12	12	9	9
Silver acetate	10	8	10	9	8
Silver acetate + CHA	18	11	11	14	11
Silver benzoate	12	8	11	10	12
Silver benzoate + CHA	18	11	25	13	13
Silver carbonate	11	7	10	10	10
Silver carbonate + CHA	17	12	17	13	13
Silver iodate	7	0	0	0	0
Silver iodate + CHA	18	12	17	12	8
Silver laurate + CHA	25	13	21	15	12
Silver protein	10	0	0	0	0
Silver protein + CHA	19	11	12	12	9
Silver chloride	9	5	6	3	3
Silver chloride + CHA	18	11	17	13	13
Silver oxide	11	7	10	9	9
Silver oxide + CHA	20	10	13	12	14
Silver sulfadiazine	13	5	8	9	7
Silver sulfadiazine + CHA	16	11	15	14	13
Silver tannate + CHA	19	-	-	-	-*

* Experiment discontinued after 1 day because of poor quality coating.

Example 26

I.V. catheters fabricated of Pellethane® 2363-90A were provided with coatings including a series of antimicrobial agents. A coating solution was prepared containing 6% Dow Pellethane® 2363-80AE and the drug in a solvent comprising 5% N-ethyl-2-pyrrolidone (NEP) and 95% tetrahydrofuran (THF). When used alone, the Ag salt was used at a level of 5%. When combined with CHA, each was used at a level of 2%. The catheters were dipped in the solution to provide a uniform coating on the device and thereafter allowed to dry for 24 hours to remove the solvent.

1 cm segments of each catheter were soaked in TSB and incubated at 37°C in a water bath shaker. At intervals of 0, 3, 9, and 12 days, 3 segments were recovered from each group, placed in the center of blood agar plates seeded with 10^4 CFU of Staph. aureus, one section to a plate, and the zone of inhibition was measured after 24 hours at 37°C. Results, expressed as an average of 3 determinations, are given in the following Table XXII.

TABLE XXII

Antibacterial Efficacy of Drug Coated I.V. Catheters against Staph. aureus in Presence of Trypticase Soy Broth

Drug on Catheter	Zone of Inhibition (mm), Days			
	3	6	9	12
Chlorhexidine (CHA)	14	12	12	11
Silver acetate	9	9	9	9
Silver acetate + CHA	15	11	12	10
Silver benzoate	10	10	10	10
Silver benzoate + CHA	13	10	12	12
Silver carbonate	10	10	12	10
Silver carbonate + CHA	14	13	13	12
Silver iodate	2	0	0	0
Silver iodate + CHA	15	15	10	10
Silver laurate + CHA	26	15	15	15
Silver protein	8	0	0	0
Silver protein + CHA	15	12	15	15
Silver palmitate + CHA	26	15	15	17
Silver chloride	5	6	6	6
Silver chloride + CHA	20	13	13	14
Silver oxide	9	9	9	9
Silver oxide + CHA	13	13	12	12
Silver sulfadiazine	9	9	9	9
Silver sulfadiazine + CHA	19	14	12	12
Cuprous oxide	4	0	0	0
Cuprous oxide + CHA	17	13	12	12

Example 27

I.V. catheters fabricated of Pellethane® 2363-90A were provided with coatings incorporating a series of antimicrobial agents. A coating solution was prepared containing 3% Dow Pellethane® 2363-80AE and the drug in a solvent comprising 5% N-ethyl-2-pyrrolidone (NEP) and 95% tetrahydrofuran (THF). The AgSD was micronized; the Ag carbonate was ground thoroughly in mortar and pestle to very fine particle size. The catheters were dipped in the solution to provide a uniform coating on the device and thereafter allowed to dry to remove the solvent.

1 cm segments of each catheter were treated and tested according to the procedure set forth in Example 26. The results obtained, expressed as maximum period of retention of activity, are given in Table XXIII below.

TABLE XXIII

Retention of Antibacterial Efficacy of Different Drug Coated Catheters (Polyurethane I.V.) in TSB Culture (10^4 Staph. aureus)

Drugs in Coating Solution	Days of Activity Retained
None	0
AgSD (5%)	1
CHA (1%)	3
AgSD + CHA (1% + 1%)	5
Ag Carbonate + CHA (1% + 1%)	5

It is to be understood that the above-described embodiments are illustrative of the application of the principles of the invention. Numerous other arrangements, processes, or compositions may be devised by those skilled in the art without departing from the spirit and scope of the invention.

Claims

1. A method of preparing an infection-resistant surface, characterized by preparing a coating vehicle by dispersing a matrix-forming polymeric material selected from the group consisting of biomedical polyurethane, biomedical silicones, biodegradable polymers and combinations thereof, in at least one solvent therefor, incorporating at least one antimicrobial agent in the coating vehicle to form a coating composition, coating the surface with the coating composition, and drying the coating.

2. The method of Claim 1, characterized in that the matrix-forming polymeric material is biomedical polyurethane preferably at a concentration in the range of 1 to 10%.

3. The method of Claim 1, characterized in that the matrix-forming polymeric material is a mixture of biomedical silicone and a biodegradable polymer, preferably poly(lactic acid) at a concentration in the range of 0.2 to 2%.

4. The method of Claim 1, characterized in that the matrix-forming polymeric material is a mixture of biomedical silicone and biomedical polyurethane.

5. The method of any of Claims 1 to 4, characterized in that the solvent is selected from the group consisting of acetic acid, methyl acetate, dimethylacetamide, ethyl 2-pyrrolidone, N-(2-hydroxyethyl)-2-pyrrolidone, N-cyclohexyl-2-pyrrolidone, and combinations thereof.

6. The method according to any of Claims 1 to 5, characterized in that the antimicrobial agent is selected from the group consisting of silver and its salts, the biguanides, polymyxin, tetracycline, aminoglycosides such as tobramycin and gentamicin, rifampicin, bacitracin, meomycin, chloramphenicol, miconazole, quinolones such as oxolinic acid, norfloxacin, nalidixic acid, pefloxacin, enoxacin and ciprofloxacin, penicillins such as oxacillin and pipracil, nonoxynol 9, fusidic acid, cephalosporins, and combinations thereof.

7. The method according to Claim 6, characterized in that said silver salts are selected from the group consisting of silver acetate, silver benzoate, silver carbonate, silver iodate, silver iodide, silver lactate, silver laurate, silver nitrate, silver oxide, silver palmitate, silver protein, and silver sulfadiazine.

8. The method according to Claim 6, characterized in that the biguanide is a chlorhexidine salt and is preferably selected from the group consisting of chlorhexidine, acetate, chlorhexidine gluconate, chlorhexidine hydrochloride, and chlorhexidine sulfate.

9. The method according to Claim 6, characterized in that the antimicrobial agent is a combination of a silver salt and a biguanide, preferably a salt of chlorhexidine.

10. The method according to Claim 9, characterized in that the antimicrobial agent is a combination of silver sulfadiazine and a salt of chlorhexidine, preferably chlorhexidine acetate.

11. The method according to any preceding Claim, characterized in that the surface is a surface of a medical device such as a catheter, contraceptive, a condom, a medical glove, a wound dressing, a wound clip, an orthopedic implant, a suture, an arterial graft, or a hernia patch.

12. The method according to any one of Claims 1 to 10, characterized in that said surface is one intended to contact health care patients such as a surface of a bed pan, a table top, a patient bed, the surface of a surgical apparatus, or an operating room surface.

13. The method of any preceding Claim, characterized in that at least one antimicrobial agent is dissolved or suspended in the coating vehicle.

14. The method of any of Claims 1 to 12, characterized in that at least one antimicrobial agent is dissolved in a solvent which is miscible with the solvent for the matrix-forming polymeric material and which is

subsequently incorporated into the coating vehicle.

15. A method of preparing an infection-resistant surface comprising preparing a first coating vehicle by dispersing a biomedical polyurethane in a solvent therefor, and optionally from 0.2 to 2% polylactic acid, and incorporating therein at least one antimicrobial agent; preparing a second coating vehicle by dispersing a biomedical silicone in a solvent therefor preferably at a concentration of 0.5 to 5%; applying said first coating vehicle to the surface and allowing it to form an adherent first coating; and applying said second coating over said first coating to form a second coating adherent to said first coating.

16. The method according to Claim 15, characterized in that antimicrobial agent is a chlorhexidine salt, preferably chlorhexidine acetate, at a level in the range of 0.5 to 3% and silver sulfadiazine in an amount within the range of 0.5 to 5%.

17. The method according to Claim 15 or 16, characterized in that the first coating vehicle further comprises a biodegradable polymer.

18. An infection-resistant composition comprising a coating vehicle comprising a biomedical polyurethane in at least one solvent therefor and an antimicrobial agent.

19. A composition according to claim 18, characterized in that the antimicrobial agent is selected from the group consisting of silver and its salts, the biguanides, polymyxin, tetracycline, aminoglycosides such as tobramycin and gentamicin, rifampicin, bacitracin, neomycin, chloramphenicol, miconazole, quinolones such as oxolinic acid, norfloxacin, nalidixic acid, pefloxicin, enoxacin and ciprofloxacin, penicillins such as oxacillin and pipracil, nonoxynol 9, fusidic acid, cephalosphorins, and combinations thereof.

20. A composition according to Claim 18 or 19, characterized in that the antimicrobial agent comprises a combination of a silver salt such as silver sulfadiazine and a biguanide such as chlorhexidine acetate in an amount effective to provide sustained antimicrobial effects when the composition is applied to a surface as a coating and dried.

21. A method of impregnating expanded PTFE medical devices, particularly vascular grafts which comprise preparing a coating vehicle comprising biomedical polyurethane and a biodegradable polymer, preferably poly(lactic acid), in a solvent therefor, together with at least one member of the group consisting of chlorhexidine and its salts, and pipracil as antimicrobial agents, placing said graft in contact with the coating vehicle while under reduced atmospheric pressure, and drying the treated graft.

22. The process of Claim 21, characterized in that the coating vehicle contains 0.25 to 1% biomedical polyurethane, 0.25 to 1% poly(lactic acid), 1% chlorhexidine acetate and 3% pipracil in a solvent comprising 25% N-ethyl-2-pyrrolidone and 75% tetrahydrofuran.

23. An expanded PTFE vascular graft, a substantial proportion of the interstices of which contains a coating composition comprising, by weight, one part biomedical polyurethane, one part poly(lactic acid), one part chlorhexidine acetate, and three parts pipracil.

24. A method of preparing an infection-resistant medical device which comprises:

(a) preparing a mixture of mixture of silver or a silver salt such as silver sulfadiazine or silver carbonate and a biguanide; and

(b) applying said mixture to the surface of a medical device.

25. The method of Claim 24, wherein the mixture is affixed to the surface of the device.

26. The method of Calim 24, wherein the mixture is applied to the surface as a powder.

27. The method of Claim 24, wherein the mixture is applied as an ingredient of a polymeric coating.

28. A method of preparing an infection-resistant medical device which comprises:

(a) preparing a mixture of

(i) a substance selected from the group consisting of chlorhexidine and its salts; and

(ii) a silver salt selected from the group consisting of silver sulfadiazine, silver acetate, silver benzoate, silver iodate, silver laurate, silver protein, silver chloride, silver palmitate, silver oxide, silver carbonate and silver nitrate; and

(b) applying the mixture to the surface of a medical device.

29. A method of preparing an infection-resistant medical device which comprises:

(a) preparing a mixture of chlorhexidine acetate and silver sulfadiazine, in proportions by weight ranging from 1:9 to 9:1; and

(b) applying the mixture to the surface of a medical device, the mixture being present at a level on the surface to impart substantial antimicrobial activity thereto.

30. The method of Claim 29, characterized in that the mixture is present in a coating on the surface at a level in the range of 10 to 70% by weight.

31. A method according to Claim 24, which comprises:

(a) preparing a powdered mixture of

(i) a member of the group consisting of chlorhexidine and its salts; and

(ii) a silver salt selected from the group consisting of a silver salt selected from the group consisting of silver sulfadiazine, silver oxide, silver carbonate and silver nitrate, silver acetate, silver benzoate, silver iodate, silver laurate, silver protein, silver chloride, silver palmitate;

(b) treating a surface of a medical device to render it at least slightly adhesive; and

(c) applying said powdered mixture to the surface of the medical device in a manner to cause adhesion to the powder thereto.

32. A method according to Claim 31, characterized in that the medical device is a glove, such as a latex

glove.

33. The method of Claim 32, where the glove is a thermoplastic latex and characterized in that the powder is applied to the glove at a point in the manufacturing process where the glove surface is soft, whereby the power particles adhere to the glove surface.

34. A method according to Claims 31, 32 or 33, characterized in that the mixture is applied by spraying a dry powdered mixture of dusting powder, a silver salt, and a biguanide.

35. A method according to Claim 31 or 32, characterized in that the mixture is applied by dipping the device into an aqueous or alcoholic slurry of dusting powder, a silver salt, and a biguanide.

36. A method of imparting infection-resistance to medical devices comprised of expanded PTFE materials comprising the step of applying to the device a coating vehicle comprising a biodegradable polymer, a silver salt and a biguanide.

37. A method of coating medical devices comprised of expanded PTFE materials to impart infection-resistance thereto comprising the steps of first dipping the device into a suspension of sodium sulfadiazine, chlorhexidine acetate and biodegradable polymer in alcohol-tetrahydrofuran (10:90), followed by a second step of dipping the device into alcoholic silver nitrate solution.

38. The method of Claims 1, 3, 4 or 15 to 17, characterized in that the coating vehicle comprises a room temperature-curing biomedical silicone.

39. The method of Claim 1, 3, 4 or 15 to 17, characterized in that the coating vehicle comprises a mixture of a polydimethyl siloxane medical adhesive and a silicone fluid comprising an amino functional polydimethyl siloxane copolymer and mixed aliphatic and isopropanol solvents.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 337 617 A2**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: 89302774.8

(22) Date of filing: 21.03.89

(51) Int. Cl.4: A61B 17/42 , A61B 10/00 , A61D 1/08 , A61D 7/02 , F16K 15/14

(30) Priority: 12.04.88 GB 8808572

(43) Date of publication of application: 18.10.89 Bulletin 89/42

(84) Designated Contracting States: AT BE CH DE ES FR GR IT LI LU NL SE

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(54) Pressure actuated valve particularly for biological use.

(57) The present invention provides a single channel needle assembly particularly for the recovery of a biologically active component such as a human embryo, which assembly comprises a single channel transcutaneous needle (1),
a three-way connector assembly (2) operatively associated with a remote end of said needle; wherein one channel (4) of said three-way assembly (2) is obturated by a valve assembly (5) comprising a resilient membrane (10) provided with at least one slit (6.7.) held under tension across said channel, said resilient membrane being arranged such that the slit remains closed during normal aspiration.

The invention also provides a method for the recovery of a biologically active component utilising the single channel needle assembly as described.

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PRESSURE ACTUATED VALVE PARTICULARLY FOR BIOLOGICAL USE

The present invention relates to a pressure actuated valve particularly for biological use.

Pressure actuated valves are known in the art. Such valves are adapted to open when a predetermined pressure differential has been established, and to close when such differential is removed, see for e.g. US-A-3734126. With delicate biological materials, however, the moving parts associated with such valve assemblies render them quite unsuited for use since the protrusions and associated parts tend to damage biological material; particularly sensitive biological material such as oocytes. According, therefore, to an aspect of the invention there is provided a pressure actuated valve characterised by a resilient membrane having at least one slit and held across a fluid pathway under tension, whereby a pressure above a threshold value is required to open the slit.

The pressure may be positive or negative and may be exerted upstream or downstream of the valve so as to exceed the threshold value. Where such pressure differentials are exerted it is possible to arrange that only one of the positive or negative pressures actuate the valve. This may be effected by arranging that the slit portions of the membrane are not merely planar, but overlap at a pre-determined side.

The membrane may have a single or multiple slit therein and may be formed of one or a plurality of layers, which layers may be conveniently utilised to form the overlapping embodiment. By utilising overlapping slits a one-way facility can be provided according to the sides the overlapping slits are applied and the direction, upstream or downstream, from which the pressure is applied.

In a particular embodiment the valves of the invention are applied to a biologically active component, e.g. an oocyte, recovery device. Accordingly, there is provided a single channel needle assembly for the recovery of a biologically active component, which assembly comprises:
a single channel transcutaneous needle,
a three-way connector assembly operatively associated with a remote end of said needle;
characterised in that one channel of said three-way assembly is obturated by a valve assembly comprising a resilient membrane provided with at least one slit held under tension across said one channel, said resilient membrane bring arranged such that the slit remains closed during normal aspiration. In such an arrangement the three-way connector is preferably connected between the remote end of the needle and a collection channel leading to a collection vessel. The third channel is a flushing channel provided with a membrane valve as just described. By this means the pressure from a hypodermic syringe, for example, is sufficient to deform the membrane to allow the flushing solution to enter the needle. When flushing has been completed a negative pressure may be applied to aspirate the collection channel which draws a biological component into a collecting vessel via the collecting channel, without emptying the flushing channel because this is closed by the membrane valve. It is most desirable that the valve is flushed with the sides of the main channel in the three-way connector so that no protruburances which might damage the oocyte are present. By this means the oocytes can be withdrawn past the entrance to the flushing channel without bruising and without the possibility that they will be taken up into the flushing channel.

In another aspect of the invention there is provided a method for the recovery of a biologically active component, which method comprises;
inserting a single channel needle assembly into the body to a site juxtaposed said component,
introducing a flushing solution into the body via said needle, and aspirating said component via said single channel;
characterised in that the remote end of the needle is operatively associated with a three-way valve assembly, said valve assembly being provided in one channel with a resilient membrane provided with at least one slit held under tension across said one channel, said resilient membrane being arranged such that said slit remains closed during normal aspiration, but opens under pressure from said flushing solution.

In a final aspect of the invention there is provided a method of inducing pregnancy in an infertile mammalian female, which method comprises recovering an oocyte from the follicle by inserting a single channel needle assembly into the ovarian follicle, introducing a flushing solution into the follicle via said needle, aspirating said component via said single channel, causing said oocytes to be fertilised in vitro and implanting said fertilised oocytes into the uterine endometrium to establish pregnancy,
characterised in that the recovery of the oocytes is effected by an arrangement wherein the remote end of the needle is operatively associated with a three-way valve assembly, said valve assembly being provided in one channel with a resilient membrane provided with at least one slit held under tension across said one channel, said resilient membrane being arranged such that said slit remains closed during normal aspiration, but opens under pressure from said flushing solution in use.

The invention will now be described, by way of illustration only, with reference to the accompanying drawings wherein:

Figure 1 shows in vertical cross-section a three-way collector incorporating a valve assembly in accordance with the present invention, and

Figures 2 and 3 show plan views from above of valve membranes in accordance with the present invention.

In accordance with the present invention, and with reference to Figure 1, a three-way connector 2 formed of a trans parent plastics material is provided with a longitudinal channel 9. Said channel 9 is a sliding fit relative to the one end of a transcutaneous single lumen needle 1, and in respect of a collecting channel catheter 3. As an initial point of assembly the needle 1 and the channel 3 are urged into sliding abutment with the body of the three-way connector 2.

The body of the three-way connector 2 is provided with an upstanding triangular portion 2a which in turn supports a flushing channel 4 which passes through the body of the support 2a and terminates between the respective ends of the needle 1 and the channel 3. Positioned at this point of juncture is the valve 5. The flushing channel 4 may of course meet the channel 3 at any desired angle, for example 90°, if the design of the portion 2a is amended.

The valve 5, as may be seen from Figures 2 and 3, may be formed of a supporting annulus 8 which holds a membrane 10 under tension. With reference to Figure 2 plane slits are made in the membrane 10. In Figure 3 overlapping portions 7 replace the plane slits 6 whereby the threshold pressures required to open the slits will be different depending on the direction from which the pressure is applied.

The arrangements as just described are particularly useful in oocyte recovery which is a procedure used in both in-vitro fertilisation and gamete intrafallopian transfer techniques. In these techniques the needle 3 is passed by transcutaneous puncture and is directed by ultrasound or laparscopy to an ovarian follicle. The follicle is punctured by the needle in order to aspirate the oocytes via the needle to a collection vessel.

Previously there have been two types of oocyte recovery needles in use: single channel as hereinbefore described, and double channel. In both cases a Heparinised solution is introduced to flush oocytes from the follicles. Although a double channel needle makes aspiration of the freed oocytes more readily achieved, it also means a larger diameter needle which increases trauma during its introduction and also on puncture of the follicle. Further, the application of negative pressure to the aspirating channel of the double channel needle can result in oocytes being lodged in the Heparin channel thereby resisting aspiration. For this reason a single channel needle tends to cause less problems in that its introduction and follicle puncture can be achieved with less trauma. In this arrangement Heparin is expressed through the needle via the flushing channel 4. In this process the collection channel 3 is temporarily obturated by compression, allowing the Heparin solution to pass to the follicles. This may be achieved because Heparin from a hypodermic syringe, for example, can be introduced under pressure down the flushing tube 4, the pressure exceeding the threshold pressure and thereby allowing the Heparin solution to pass into the lumen of the needle 1. When a sufficiency of Heparin solution has passed down the needle 1 the oocytes are withdrawn by aspiration along the collecting channel 3. The negative pressure applied is below the threshold value of the valve membrane 5 and, with the compression removed, the aspirated Heparinised solution bearing oocytes is withdrawn to the collecting vessel. This arrangement prevents the oocytes from passing into the channel 4, avoids bruising them, and prevents Heparinised solution remaining in the channel 4 from flowing into the collection vessel. This is important because it is only possible to correctly aspirate the follicle if the valve 5 is closed.

Accordingly, the invention provides a pressure actuated valve as hereinbefore described, a membrane for such a valve, and a method for the operation of a presure actuated valve.

Claims

1. A single channel needle assembly for the recovery of a biologically active component, which assembly comprises;
a single channel transcutaneous needle (1),
a three-way connector assembly (2) operatively associated with a remote end of said needle;
characterised in that one channel (4) of said three-way assembly (2) is obturated by a valve assembly (5) comprising a resilient membrane (10) provided with at least one slit (6.7.) held under tension across said one channel, said resilient membrane being arranged such that the slit remains closed during normal aspiration.

2. An assembly as claimed in claim 1 characterised in that the membrane is formed with at least two layers with slits (7) out of register but in communication, thereby to form an overlap slit.

3. An assembly according to claim 2 wherein the slits overlap to provide different pressure thresholds at upstream and downstream sides of the membrane.

4. A method for the recovery of a biologically active component, which method comprises;
inserting a single channel needle assembly into the body to a site juxtaposed said component,
introducing a flushing solution into the body via said needle, and aspirating said component via said single channel;
characterised in that the remote end of the needle (1) is operatively associated with a three-way valve assembly (2), said valve assembly being provided in one channel (4) with a resilient membrane (5) provided with at least one slit (6.7.) held under tension across said one channel, said resilient membrane being arranged such that said slit remains closed during normal aspiration, but opens under pressure from said flushing solution.

5. A method according to claim 4 characterised in that the component is a mammalian oocyte, and wherein the flushing solution is introduced by obturating the aspiration channel prior to introduction of the flushing solution under pressure.

6. A method of inducing pregnancy in an infertile mammalian female, which method comprises recovering an oocyte from the follicle by inserting a single channel needle assembly into the ovarian follicle,
introducing a flushing solution into the follicle via said needle, aspirating said component via said single channel, causing said oocytes to be fertilised in vitro and implanting said fertilised oocytes into the uterine endometrium to establish pregnancy, characterised in that the recovery of the oocytes is effected by an arrangement wherein the remote end of the needle (1) is operatively associated with a three-way valve assembly (2), said valve assembly being provided in one channel (4) with a resilient membrane (5) provided with at least one slit (6.7.) held under tension across said one channel, said resilient membrane being arranged such that said slit remains closed during normal aspiration, but opens under pressure from said flushing solution in use.

7. A method according to claim 6 characterised in that the solution is a heparinized solution.

FIG.1

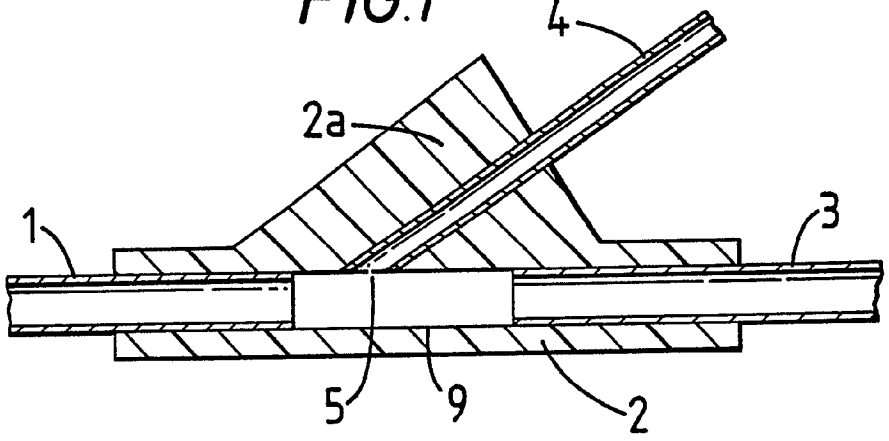


FIG.2

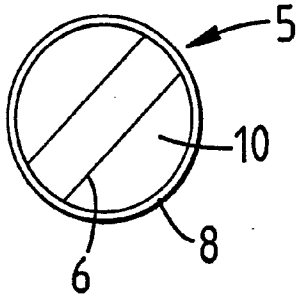
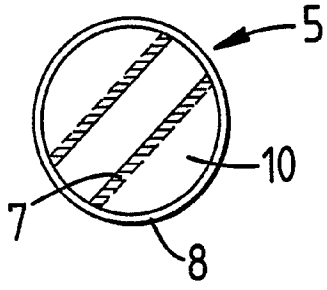


FIG.3



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number : **0 589 577 A1**

(12) EUROPEAN PATENT APPLICATION

(21) Application number : **93306928.8**

(22) Date of filing : **01.09.93**

(51) Int. Cl.[5] : **A61M 16/00**

(30) Priority : **24.09.92 US 949978**

(43) Date of publication of application :
30.03.94 Bulletin 94/13

(84) Designated Contracting States :
DE ES FR IT SE

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(54) Suction catheter assemblies.

(57) A closed system suction catheter assembly has a protective sleeve 2 enclosing an aspirating catheter 1 extending though a sliding seal 50 in a patient coupling 4. The catheter 1 has an antimicrobial surface such as formed by silver sulfadiazine which reduces the accumulation of bacteria and prolongs the useful life of the assembly.

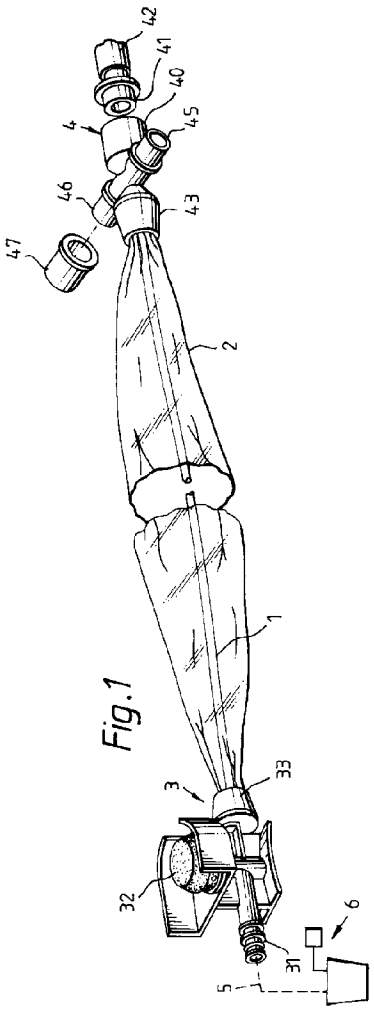

Fig.1

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This invention relates to suction catheter assemblies of the kind for use in removing undesirable fluid from the respiration passages of a patient, the catheter assembly including an aspirating catheter having a proximal end and a distal end suitable for insertion into a patient, a vacuum coupling located in the vicinity of the proximal end of the aspirating catheter, a patient coupling mounted to surround the aspirating catheter in the vicinity of the distal end of the aspirating catheter, and a flexible protective sleeve extending along the aspirating catheter where it extends between the patient coupling and the vacuum coupling, and the patient coupling having a sliding seal with the external surface of the aspirating catheter such that the catheter is wiped by the seal as it is advanced and withdrawn periodically through the sliding seal into the protective envelope.

In such assemblies the patient coupling has one port connected to a tracheal tube and two further side ports by which ventilation of the patient can take place. In use, the machine end of the catheter is connected to a suction source via a valve. Secretions that build up on the inside of the tracheal tube, the trachea and bronchi can be periodically removed by advancing the catheter through the coupling and down the tracheal tube and opening the valve. The coupling enables ventilation of the patient to continue while suctioning takes place.

Examples of catheter assemblies having an aspirating catheter which is contained within a sleeve and which can be pushed through a sliding seal on a coupling are described in several patents, such as US 3,991,752 to Radford; US 4,569,344 to Palmer; US 4,638,539 to Palmer; US 4,696,296 to Palmer; US 4,825,859 to Lambert; US 4,834,726 to Lambert; US 4,836,199 to Palmer; US 4,838,255 to Lambert; US 4,872,579 to Palmer; US 4,938,741 to Lambert; US 4,967,743 to Lambert; US 4,981,466 to Lambert; US 5,025,806 to Palmer; US 5,029,580 to Radford; US 5,060,646 to Page; US 5,065,754 to Jensen; US 5,073,164 to Hollister; and GB 2207736 to Hollister. Suction catheter assemblies of this kind are also available from Smiths Industries Medical Systems Inc under the trade mark STERICATH and from Ballard Medical Products Inc under the trade mark TRACHCARE.

The sliding seal in the assembly removes some of the secretions clinging to the outside of the aspirating catheter each time it is withdrawn but, nevertheless, some will remain on the external surface of the catheter. These secretions contain microbes from the patient that can colonize to larger populations and present a potential risk to the patient on reintroduction of the catheter. In some assemblies, irrigating fluid can be applied to the outside of the catheter which helps remove secretions but does not completely remove them.

The environment within the protective sleeve encourages the multiplication of bacteria on the outside of the catheter and, for this reason, the time for which the suction catheter assembly can be used is generally limited to about 24 hours. This is a disadvantage because each time the assembly has to be removed and replaced, ventilation of the patient must be interrupted. The opening of the ventilation circuit can allow external microbes to be introduced into the patient causing nosocomial infections. Also, the repeated replacement of the assemblies leads to increased cost and waste, with the consequent disposal difficulties involved with soiled surgical products. Closed system suction catheter assemblies have considerable advantages to the user compared with conventional suction catheters so it is highly desirable for the cost of using the assemblies to kept as low as possible in order to encourage their use. Any assembly which can be used safely for a longer period would, therefore, bring with it cost savings and advantages to the patient.

It is an object of the present invention to provide a suction catheter assembly which can be used for a longer period.

According to one aspect of the present invention there is provided a tracheal suction catheter assembly of the above-specified kind, characterised in that the aspirating catheter has at least an external surface with antimicrobial properties that minimize the accumulation of bacteria on the external surface of the catheter.

According to another aspect of the present invention there is provided a suction suction catheter assembly for use in removing undesirable fluid from a patient, the catheter assembly including an aspirating catheter having a proximal end and a distal end suitable for insertion into a patient, a vacuum coupling located in the vicinity of the proximal end of the aspirating catheter, a patient coupling mounted to surround the aspirating catheter in the vicinity of the distal end of the aspirating catheter, the patient coupling having a sliding seal with the external surface of the aspirating catheter, and a protective sleeve extending along the aspirating catheter where it extends between the patient coupling and the vacuum coupling, characterised in that the assembly has an antimicrobial substance on a component of the assembly that is effective to reduce transfer of bacteria from the external surface of the catheter to the patient.

The antimicrobial surface is preferably provided by an antimicrobial substance incorporated within the wall of the catheter. Alternatively, an antimicrobial coating could be formed by a coating on the external surface of the catheter. The antimicrobial surface may be provided by a substance including a silver compound such as silver sulfadiazine. The antimicrobial substance may include a silver compound with a binder such as alumino-silicate or hydroxyapitate. Alternatively, the antimicrobial substance may include

a silver compound with a polymer attachment substace. The antimicrobial substance may include chlorhexidene. The aspirating catheter may be substantially of PVC.

It has previously been proposed to coat catheters which remain in the body for prolonged periods with an antimicrobial substance so as to reduce the risk of infection. Examples of these previous catheters include urinary catheters and venous catheters (such as the Arrow Antiseptic Multi-Lumen Central Venous Catheter). These catheters remain in the body and are disposed of after use. By contrast, in the present invention the catheter remains outside the body for the majority of the time and is periodically inserted and removed through a sliding seal. It has been discovered that an antimicrobial surface on an aspirating catheter is effective to reduce the build up of bacteria outside the body and that the antimicrobial properties remain effective even though the catheter passes repeatably through a sliding seal.

A suction catheter assembly according to the present invention, will now be described, by way of example, with reference to the accompanying drawings, in which:

Figure 1 is a perspective view of the assembly; and

Figure 2 is a sectional view of the assembly; to a larger scale.

The suction catheter assembly comprises an aspirating catheter 1 that extends within a flexible, protective sleeve 2 between a vacuum connecting member 3 and a patient connecting member 4.

The aspirating catheter 1 has an outside diameter of about 4-5mm and a length of about 55cm. In the illustrated example, the catheter 1 has a single lumen 10 although catheters with multiple lumens for use in irrigation, oxygen supply or medication delivery could be used. At its machine or proximal end, the catheter 1 is secured to the vacuum connecting member 3.

The vacuum connecting member 3 is moulded from a rigid plastics material and has a bore (not shown) extending along it into one end of which the catheter 1 is bonded. The opposite end of the bore extends through a spigot 31 which, in use, is connected to tubing 5 which extends to a vacuum or suction source 6. The vacuum connecting member 3 includes a conventional manually-operated valve 32 which normally prevents flow through the connecting member 3 and catheter 1 but which can be pressed down by the user to open the valve and connect the lumen 10 of the catheter to the suction source 6.

The proximal end of the sleeve 2 is secured to the vacuum connecting member 3 beneath a threaded collar 33 secured to the distal end of the vacuum connecting member. The distal end of the sleeve 2 is similarly secured to the patient connecting member 4 by means of a threaded collar 43 which is screwed onto a threaded, proximal extension 44 of the patient connecting member.

The patient connecting member 4 is of generally cruciform shape. At its distal, or patient end, the connecting member 4 has a female luer coupling 40 which is aligned with the axis of the member and with the proximal extension 44. The coupling 40 is adapted to be connected to a cooperating coupling 41 on the end of a tracheal tube 42. Two side ports 45 and 46 extend at right angles to the axis of the connecting member, directly opposite one another, about midway along the length of the connecting member. These two side ports 45 and 46 communicate directly with the interior of the coupling 40 and are used in the conventional manner to connect with ventilation apparatus. One port may be used for inhalation gas and the other port used for exhalation gas. Alternatively, one of the ports 46 may be closed by a cap 47 and inhalation and exhalation both be effected through the other port 45.

The patient connecting member 4 includes a sliding seal 50 in the form of a resilient diaphragm with a central aperture 51 through which extends the aspirating catheter as a close sliding fit.

The aspirating catheter 1 is mainly of PVC but contains an antimicrobial substance so that it has an external surface 11 which has antimicrobial properties. The antimicrobial substance is blended with polymer pellets, in a proportion of about 3-10% by weight substance to polymer, prior to extrusion of the catheter so that the wall of the catheter is antimicrobial throughout its thickness and has antimicrobial properties on both its internal and external surfaces. Alternatively, the external antimicrobial surface may be formed by coating or otherwise forming an antimicrobial layer on the external surface only.

The antimicrobial substance may be silver sulfadiazine or chlorhexidine. Alternatively, a silver ion with a binder such as alumino-silicate, hydroxyapatite or a polymer attachment substance such as polyurethane could be used. Combinations of these materials, such as, silver sulfadizine and chlorhexidine could also be used.

In operation, the coupling 40 of the connecting member 4 is secured to a coupling 41 on the end of a tracheal tube 42 and its side ports 45 and 46 are connected to a ventilator. The vacuum coupling member 3 is connected to the suction source 6 but, as long as the manual valve 32 remains unactuated, no suction is applied to the catheter 1.

When aspiration of fluid from the trachea or bronchi is required, the user grips the catheter 1 through the sleeve 2 and pushes it forwardly so that the distal, patient end of the catheter is advanced through the connecting member 4 and into the tracheal tube 42. When the catheter 1 has been inserted to the desired depth, the user depresses the valve 32 so that the catheter is connected to the suction source 6 and fluid in the vicinity of the tip of the catheter is sucked into

the catheter and removed. During aspiration, ventilation of the patient occurs normally. When aspiration is complete, the catheter 1 is pulled back into the sleeve 2, the assembly remaining attached to the tracheal tube connector so that it can be reused when necessary.

It has been found that the antimicrobial properties of the external surface 11 remain effective for a prolonged period despite being repeatedly displaced backwards and forwards through the sliding seal 50. The antimicrobial surface 11 minimizes the growth of bacteria on the catheter and enables the assembly to be used for periods of up to about 48 hours depending on how frequently the assembly is used. This is considerably longer than an equivalent assembly without any antimicrobial treatment which might typically be used for about 24 hours.

Alternative assemblies may include an antimicrobial substance on another component of the assembly that is effective to reduce transfer of bacteria from the catheter to the patient. For example, an antimicrobial substance on the inside of the sleeve 2 may help reduce microbial accumulation on the external surface of the catheter because of contact of the sleeve with the catheter during handling. Alternatively, an antimicrobial substance in the sliding seal 50 might help reduce transfer of bacteria from the catheter to the patient as the catheter is pushed through the seal.

Claims

1. A tracheal suction catheter assembly for use in removing undesirable fluid from the respiration passages of a patient, the catheter assembly including an aspirating catheter (1) having a proximal end and a distal end suitable for insertion into a patient, a vacuum coupling (3) located in the vicinity of the proximal end of the aspirating catheter (1), a patient coupling (4) mounted to surround the aspirating catheter in the vicinity of the distal end of the aspirating catheter, and a flexible protective sleeve (2) extending along the aspirating catheter (1) where it extends between the patient coupling (4) and the vacuum coupling (3), and the patient coupling having a sliding seal (50) with the external surface (11) of the aspirating catheter such that the catheter is wiped by the seal as it is advanced and withdrawn periodically through the sliding seal into the protective envelope (2), characterised in that the aspirating catheter (1) has at least an external surface (11) with antimicrobial properties that minimize the accumulation of bacteria on the external surface of the catheter (1).

2. A suction catheter assembly for use in removing undesirable fluid from a patient, the catheter assembly including an aspirating catheter (1) having a proximal end and a distal end suitable for insertion into a patient, a vacuum coupling (3) located in the vicinity of the proximal end of the aspirating catheter (1), a patient coupling (3) mounted to surround the aspirating catheter (1) in the vicinity of the distal end of the aspirating catheter, the patient coupling (4) having a sliding seal (50) with the external surface (11) of the aspirating catheter, and a protective sleeve (2) extending along the aspirating catheter where it extends between the patient coupling (4) and the vacuum coupling (3), characterised in that the assembly has an antimicrobial substance on a component (1) of the assembly that is effective to reduce transfer of bacteria from the external surface (11) of the catheter (1) to the patient.

3. A suction catheter assembly according to Claim 1 or 2, characterised in that the antimicrobial surface is provided by an antimicrobial substance incorporated within the wall of the catheter (1).

4. A suction catheter assembly according to Claim 1 or 2, characterised in that the antimicrobial surface is provided by a coating on the external surface (11) of the catheter (1).

5. A suction catheter assembly according to any one of Claims 1 to 4, characterised in that the antimicrobial surface is provided by a substance including a silver compound.

6. A suction catheter assembly according to Claim 5, characterised in that the antimicrobial substance includes silver sulfadiazine.

7. A suction catheter assembly according to Claim 5 or 6, characterised in that the antimicrobial substance includes a silver compound with a binder.

8. A suction catheter assembly according to Claim 7, characterised in that the binder is selected from the group comprising alumino-silicate and hydroxyapatite.

9. A suction catheter assembly according to Claim 5 or 6, characterised in that the antimicrobial substance includes a silver compound with a polymer attachment substance.

10. A suction catheter assembly according to any one of the preceding claims, characterised in that the antimicrobial substance includes chlorhexidene.

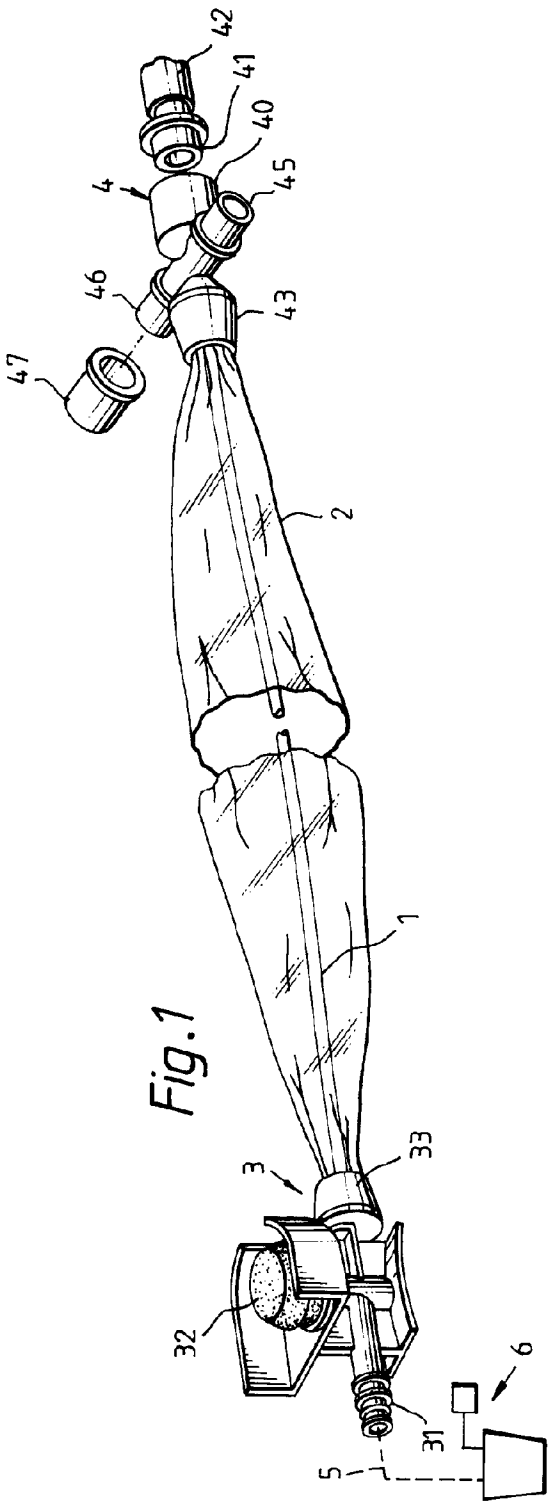

Fig.1

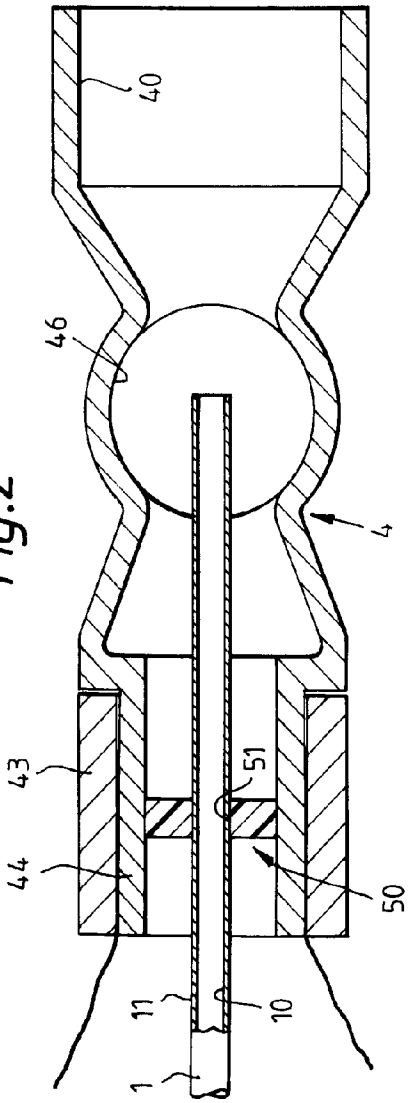

Fig.2

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 93 30 6928

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
D,Y	US-A-5 073 164 (HOLLISTER) * abstract; figures 1,3 *	1-4	A61M16/00
Y	DE-A-34 35 553 (SIEMENS) * the whole document *	1-4	
A	DE-A-33 02 567 (STEIDLE) * claims 1,4,7,9; figure 1 *	1-5	
A	US-A-4 581 028 (FOX) * abstract *	5,6	
A	WO-A-90 01956 (SMITH & NEPHEW) * abstract *	10	
A	EP-A-0 229 862 (TERUMO KABUSHIKI KAISHA) * abstract *	1-3	
			TECHNICAL FIELDS SEARCHED (Int.Cl.5)
			A61M

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	29 November 1993	Kousouretas, I

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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EPO FORM 1503 03.82 (P04C01)

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 864 336 A2

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
16.09.1998 Bulletin 1998/38

(51) Int Cl.[6]: **A61M 25/00**

(21) Application number: **98301737.7**

(22) Date of filing: **10.03.1998**

(84) Designated Contracting States:
AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **10.03.1997 US 813935**

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(54) Catheter with valve mechanism

(57) A catheter (10) having a closed distal end and one or more valve mechanisms in the form of slits (22) adjacent the distal end which communicate the lumen (24) extending through the catheter with the exterior of the catheter to permit the infusion or aspiration of fluids between the catheter and the vessel in which the catheter is positioned. The or each valve mechanism (22) is preferably in a plane which is oriented at an angle to the longitudinal axis of the catheter (10), and is preferably in an area of reduced wall thickness to facilitate opening and closing.

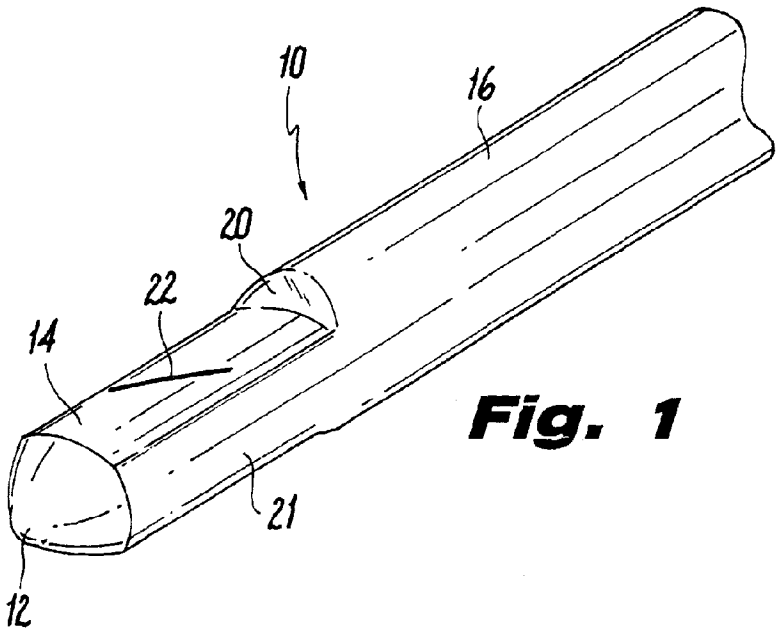

Fig. 1

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Description

This invention relates to catheters incorporating a valve mechanism to permit the ingress and egress of fluids therethrough into and out of the body of a patient.

The use of catheters in intravenous procedures and for intravenous therapies is well known in the medical community. Catheters typically are implanted into various vessels in the patient's body to provide for the ingress and/or egress of fluids, such as blood and other bodily fluids, and as well for the infusion of medication or other medical solutions for both specific treatment of the patient and to facilitate other treatments and diagnoses. The use of catheters may be for short term procedures, but they are also commonly used in long term procedures wherein the catheter is implanted in the body and left in place for an extended period of time to facilitate long term treatment of the patient.

Catheters typically take the form of an elongated tube constructed of a biocompatible surgical grade material which is flexible to permit guiding or steering of the catheter through blood vessels or anatomical passages. Initially, catheters generally included an open ended tube which was positioned during the surgical procedure, and was capped at its proximal end (i.e. the end positioned outside the body) to provide a port for the infusion or withdrawal of fluids. The distal end of the catheter remained open inside the vessel within the patient's body, and allowed for ready withdrawal or infusion of fluids through the catheter. These catheters were typically used in short term procedures, such as surgical procedures in which the catheter would be removed after completion of the surgical procedure. Leaving a catheter of the open-ended type in the vessel of the patient subjected the catheter to a number of potential problems, including the formation of blood clots which would obstruct the end of the catheter. Open-ended catheters are thus flushed regularly, typically with a saline and/or anticoagulant solution, to keep the distal end of the catheter open.

Catheters intended to remain in the body for a longer term have been developed and generally include a closed distal end and a valve adjacent the distal end to permit the infusion or withdrawal of fluids. Typically, these valves operate by reacting to the pressure differential within the tube as compared to the vessel (or other anatomical location) in which the catheter is placed. Generally, increasing the pressure within the catheter provides for infusion of fluids through the valve and into the vessel, while a pressure decrease in the catheter provides for withdrawal of the fluids from the site in which the catheter is placed.

A challenge associated with closed end catheters having valves adjacent their distal end is the performance of the valve based on a pressure differential. Although efforts have been made to optimize the performance of such valved catheters, e.g. by chemical weakening the area of the catheter tube adjacent to the valve or other localized treatment as disclosed in US patent Nos. 4,549,879, 4,701,166, 4,995,863 and 5,147,332 a need remains to further optimize the fabrication and/or performance of existing valved catheters.

According to the invention, there is provided a catheter comprising an elongated member with a lumen extending therethrough characterised in that the elongated member has a portion of reduced diameter extending along a portion of its length with at least one valve mechanism therein, wherein the valve mechanism is oriented at an angle to the longitudinal axis of the elongated member and opens in response to positive or negative pressure to allow the egress and ingress of fluid through the lumen.

Preferably, the or each valve mechanism is a slit valve.

The preferred catheter comprises an elongate flexible tube which is fabricated from a surgical grade material and has an open and closed end. The catheter tube has a wall which is defined by an inner and outer surface of the tube, where the inner surface of the tube is defined by a lumen which extends the length of the tube. In one preferred embodiment, when viewed in cross-section at two different longitudinal points, at least a portion of the tube at the more distal point has a reduced thickness with respect to the tube when viewed at a more proximal point, and at least one valve mechanism is positioned solely or entirely in this portion of reduced thickness to place the lumen in communication with the exterior of the tube.

The reduced thickness portion of the catheter tube, in a further embodiment, is the result of the lumen of the catheter tube being offset and parallel to the longitudinal axis of the tube, and in another embodiment is the result of the lumen having an oval cross-section such that the major axis of the oval defines the portions of reduced thickness in the wall of the tube. In each of these cases, the valve mechanism is provided in the portion or portions of reduced thickness, and does not extend into the areas of increased thickness so that the operation of the valve is consistent along its length.

In an alternate embodiment of the present catheter, the valve mechanism comprises at least one pair of slits which are parallel to each other but still positioned at an angle to the longitudinal axis of the catheter tube. Preferably, the slits, when formed through the tube, are cut at different angles relative to the catheter tube wall surface to facilitate the infusion or withdrawal of fluids.

In each of the embodiments, it is preferred that the valves positioned at an angle to the longitudinal axis of the catheter are located in the area of reduced thickness to increase the size of the opening for the ingress and egress of fluids.

Other features of the catheter of the present invention will become apparent from the detailed description hereafter of preferred embodiments given by way of example only with reference to the accompanying drawings, in which:

Figure 1 is a perspective view of a catheter according to a first embodiment of the invention;
Figure 2 is a top plan view of the catheter of Figure 1;
Figure 3 is a side elevation view of the catheter of Figure 1;
Figure 4 is a side cross-section view of the catheter of Figure 1 taken along lines 4-4 of Figure 2;
Figure 5 is a perspective view of a catheter according to a second embodiment;
Figure 6 is a side elevation of the catheter of Figure 5;
Figure 7 is a side cross-sectional view of the catheter of Figure 5 taken along lines 7-7 of Figure 6;
Figure 8 is a front elevation view of the catheter of Figure 5;
Figure 9 is a perspective view of a catheter according to a third embodiment;
Figure 10 is a top plan view of the catheter of Figure 9;
Figure 11 is a cross-sectional view of the catheter of Figure 9 taken along lines 11-11 of Figure 10 showing a circular lumen;
Figure 12 is a cross-sectional view similar to Figure 11 showing an oval lumen;
Figure 13 is a perspective view of a catheter according to a fourth embodiment;
Figure 14 is a side elevation view of the catheter of Figure 13;
Figure 15 is a cross-sectional view of a catheter similar to Figure 13 except that the two slits of each valve lie in planes which intersect;
Figure 16 is a perspective view of a catheter according to a fifth embodiment;
Figure 17 is a side cross-sectional view of the catheter of Figure 16 taken along lines 17-17 of Figure 16;
Figure 18 is a cross-sectional view of the catheter of Figure 16 taken along lines 18-18 of Figure 16;
Figure 19 is a perspective view of a catheter according to a sixth embodiment;
Figure 20 is a side cross-sectional view of the catheter of Figure 19 taken along lines 20-20 of Figure 19; and
Figure 21 is a cross-sectional view of the catheter of Figure 19 taken along lines 21-21 of Figure 19.

Referring now to the drawings, in which like reference numerals represent similar or identical elements throughout the several views, there is illustrated in Figure 1 a catheter 10 having a valve mechanism 22 positioned in an area of reduced thickness relative to proximal portions of catheter 10 which, in combination with its orientation to be explained hereafter, facilitates the operation of the valve mechanism to open and close for infusing or withdrawing fluids. Catheter 10 preferably is constructed of a flexible, biocompatible surgical grade material and terminates in closed distal end 12, which may take the form of an end cap 13, as seen in Figures 2-4 or may be molded as part of the catheter body 16.

Body 16 has a first diameter which corresponds to a first thickness 28, as seen in Figure 4, of the wall of the catheter 10. A transition region 20 is provided which leads to a region 14, which is preferably substantially planar and which has a second region 26 of a reduced thickness which is less than that of the first thickness 28, as best seen in Figure 4. The reduced thickness provides added flexibility to slit valves 22,23 provided therein thereby facilitating opening and closing of the valves.

Slit valves 22,23 open in response to increased or decreased pressure within lumen 24 to permit the infusion and egress of fluids into or from the catheter 10 and into the vessel in which the catheter is positioned. In the embodiment shown in Figures 3 and 4, the pair of slit valves 22,23 are cut or otherwise configured in such a manner so as to provide for infusion through one valve, i.e. valve 22, and egress through a second valve, i.e. valve 23. In other words, in this embodiment, valve 22 opens in response to increased pressure in lumen 24 and valve 23 opens in response to decreased pressure in lumen 24. Planar region 14 facilitates the opening and closing of the valves due to the reduced thickness 26 of the catheter wall, and it can be seen that, in this embodiment, the valves are positioned exclusively within the area of reduced thickness 26. In an alternate embodiment, the slit valves 22,23 are identical and the ingress and egress of fluids is through both valves.

Preferably, planar region 14 is formed in the catheter wall on diametrically opposite sides thereof. As can be seen in Figure 4, however, the reduction in wall thickness does not affect the diameter of lumen 24, which is maintained substantially constant throughout the length of catheter 10. As shown in Figure 2, the outer diameter of the catheter 10 remains constant along sides 21. Alternately, the thickness 28 of the catheter wall can be reduced circumferentially about the end of catheter 10 distally of the transition region 20, with the wall thickness being constant at this distal end of catheter 10 and the diameter of the lumen remaining constant throughout the catheter length.

Figures 1 and 2 show the valve 22 oriented at an angle to the longitudinal axis of catheter 10. Thus, valve 22 lies in a plane oriented at an angle to the longitudinal axis. Positioning the valve 22 at an angle within the reduced wall thickness results in a larger opening for the ingress and egress of fluids. When suction is applied, the reduced thickness wall will want to collapse so it will twist. Thus the slit opens into an eye-shaped opening as shown for example in Figure 18A. A preferred angular orientation of valve 22 relative to the longitudinal axis is 30 degrees, although differing angles, and particular greater angles, will provide the desired advantage.

Figures 5-8 illustrate a second embodiment of catheter 30, in which the reduced wall thickness 34 is located at the distal end of the catheter 30. Valve mechanism 36 is provided in the tapered closed distal end 34 and

permits the infusion or egress of fluids in response to an increased or decreased pressure, respectively, in the lumen of the catheter. Opening 38 permits the ingress or egress of fluids through the distal end 34.

In order to facilitate manufacture of the catheter 30, the valve 36 may be provided on a tip 30a of the catheter as shown in Figures 6-8. Tip 30a includes a catheter entrance 40 which accommodates the distal end of an open ended catheter which slips into tip 30a at entrance 40 and abuts against catheter abutment 42. Lumen 52 of tip 30a communicates with the lumen of the catheter (see Figure 7). Catheter tip 30a includes a wall 44 having a first thickness and a reduced wall thickness 46 at valve mechanism 36 whereby the valve mechanism is positioned exclusively within the area of reduced thickness 46 and in a plane which is at an angle to the longitudinal axis of the catheter, in this case perpendicular. In this Figure 7 embodiment, valve mechanism 36 further includes a hinge portion 48 which facilitates opening and closing of the valve 36, and a seal 50 which seals the opening 38 at the distal end of the catheter tip. Valve mechanism 36 will flex outwardly to permit the infusion of fluids from the catheter into the vessel in which the catheter is positioned in response to increased pressure within the lumen 52, and inwardly to permit the withdrawal of fluids from the vessel and into the lumen 52.

Turning now to Figure 9, there is illustrated another embodiment of catheter 60 in which a pair of valve mechanisms 64, preferably slits, are provided in the body 62 of the catheter 60, adjacent the closed distal end 66. Each valve mechanism 64 is positioned at an angle to the longitudinal axis of the catheter 60, and preferably at a 30° angle. Optionally, valve mechanisms 64 may be provided at angles which are opposite to each other. Preferably, each such valve mechanism is positioned at an angle of approximately 30° to the longitudinal axis. Thus, in an embodiment wherein the two valve mechanisms are oriented opposite each other, the angles would be plus and minus 30 degrees relative to the longitudinal axis, respectively.

As seen in Figures 10-12, valve mechanism 64 is positioned exclusively or wholly within reduced thickness wall portion 76 of the catheter wall 74, and is positioned at an angle to the longitudinal axis 70. The reduced wall thickness 76 is a result, as seen in Figure 11, of extruding the catheter tubing so as to have a lumen 68 which is offset from the longitudinal axis 70 of the catheter 60. In the embodiment shown in Figure 11, lumen 68 has a longitudinal axis 72 which is offset from the longitudinal axis 70 of the catheter 60. Wall 74 has a greater thickness than wall portion 76, and the valve mechanism 64 is positioned exclusively within the reduced thickness wall portion 76.

Figure 12 illustrates a further manner of extruding the catheter 60 in order to provide for the positioning of valve mechanisms 64 in the reduced thickness wall portion 76. In this embodiment, the lumen 68 has an oval cross-section, such that its longitudinal axis is aligned with longitudinal axis 70 of the catheter 60. The reduced thickness wall portions 76 are located at the ends of the major axis 78 of the oval shaped lumen 68, and the valve mechanisms 64 are provided at the end of the major axis 78.

Figures 13-15 illustrate further embodiments of catheter 80, in which the valve mechanisms 82,83 preferably comprise a pair of slits 84,84 and 86,86. In the embodiment of Figures 13 and 14, the slits of each pair are placed side by side and the planes of the slits of each pair are substantially parallel. Ingress and egress of fluids occur through both valve mechanisms 82,83.

The embodiment of Figure 15 is similar to that of Figures 13 and 14 in that each valve mechanism 82'83' preferably has a pair of slits 84',84',86',86', however, the planes of the slits of each pair intersect. In this embodiment, as best seen in Figure 15, the slits 84' are positioned side by side, spaced equidistantly along their lengths, and are cut at an angle from the outer surface 88' through wall 90' to inner surface 92' such that one of the slits 84' is cut in the direction towards the other slit 84'. Slits 84' intersect interiorly within the catheter 80 within lumen 94. When cut in this manner, valve 82' opens outwardly in response to increased pressure in the lumen 94 to permit the infusion of fluids from the lumen 94 of the catheter into the vessel in which the catheter is positioned.

As further seen in Figure 15, slits 86' of valve mechanism 83' are cut at an angle from the outer surface 88' to the inner surface 92' through wall 90' away from each other, are positioned side by side, and spaced equidistantly along their lengths. As can be seen from Figure 15, slits 86' will intersect exteriorly to the catheter 80. Thus, the valve mechanism opens inwardly in response to decreased pressure in the lumen 94 of the catheter 80 to permit the withdrawal or aspiration of fluids from the vessel into the catheter.

In addition, it can be seen in Figure 15 that increased pressure in lumen 94 will force valve 83' outwardly against wall 90', further sealing valve 83' to facilitate infusion through valve 82'. Likewise, decreased pressure in lumen 94 forces valve 82' inwardly against wall 90, further sealing valve mechanism 82' to facilitate aspiration through valve mechanism 83'.

Figures 16-18 illustrate another alternate embodiment in which a separate valve assembly 100 is mounted e.g. by insert molding, on the tip of catheter 101 to form the catheter for insertion into the body. Valve assembly 100 includes a reduced thickness area 102 around its entire circumference. Nose 104 is configured for easier penetration, is glued to the valve assembly, and seals the distal end of the catheter and assembly 100. As shown, the reduced thickness area 102 is formed by reducing the thickness of wall 105, thereby maintaining the diameter of lumen 106 constant so as not to effect flow. Note that walls 120a-120d are slightly radiused with portions 107a-d of increased wall thickness to increase stability. The transition areas 108,109

preferably slope at an angle of about 8 to about 12 degrees to maintain stability of the catheter. A pair of diametrically valve mechanisms, preferably a pair of opposed slits 110,112 are angled with respect to the longitudinal axis (illustratively at an angle of about 24 degrees) and function as described above with respect to the embodiment of Figure 1. Thus, slit valve mechanisms 110,112 open into eye-shaped openings as shown in Figure 18A.

Length L between nose 104 and transition area 108 is selected to optimize valve performance and in a 9 French catheter preferably ranges from about 0.1 to about 0.2 inches and more preferably about 0.144 inches.

Valve assembly 240 illustrated in Figures 19-21 is identical to the valve assembly 100 of Figures 16-18 except that the reduced thickness area 202 is circular in cross section. As shown, area 202 is formed by reducing the thickness of wall 205 without effecting the internal diameter of lumen 206. Nose 204 is affixed in the same manner as nose 104. Valve mechanisms 210,212, shown as slits, are illustratively angled at about 24 degrees. As with the aforementioned embodiments, other angles are contemplated.

As noted above, the combination of an angled slit disposed on a region of reduced thickness results in a larger opening. Figure 18A illustrates by way of example the resulting eye shaped opening O which can be achieved.

Claims

1. A catheter having a lumen (24) extending therethrough **characterised in that** the catheter has a portion (14) of reduced diameter extending along a portion of its length with at least one valve mechanism (22) therein, oriented at an angle to the longitudinal axis of the catheter which opens in response to positive or negative pressure to allow the egress and ingress of fluid through the lumen (24).

2. A catheter according to claim 1 characterised in that the reduced diameter portion (14) is circular in cross-section.

3. A catheter according to claim 1 or claim 2 characterised by an end cap (13) positioned on the distal end of the catheter to seal the distal end of the lumen (24).

4. A catheter according to any one of the preceding claims characterised in that the lumen (70) is tubular and has a circular cross-section, the longitudinal axis of the lumen being offset and parallel to the longitudinal axis of the catheter to define a portion (76) of reduced thickness in the wall (74) of the catheter.

5. A catheter according to any of claims 1-3 characterised in that the lumen (70) has an oval cross-section, the longitudinal axis of the lumen being aligned with the longitudinal axis of the catheter, such that the major axis of the oval defines portions (76) of reduced thickness in the wall of the catheter.

6. A catheter according to any one of the preceding claims characterised in that the valve mechanism (22) is oriented at an angle of approximately 30° to the longitudinal axis of the catheters.

7. A catheter according to any one of the preceding claims further characterised by a second valve mechanism (23) which is oriented at an angle of approximately 150° to the longitudinal axis of the catheter.

8. A catheter according to claim 5 further characterised by a second valve mechanism (64), the first valve mechanism (64) being positioned at one end of the major axis of the oval cross-section and the second valve mechanism (64) being positioned at a second end of the major axis.

9. A catheter according to claim 8 characterised in that the first valve mechanism is oriented at an angle of approximately 30° to the longitudinal axis of the catheter and the second valve mechanism is oriented in a plane which is at an angle of approximately 150° to the longitudinal axis of the catheter.

10. A catheter according to claim 7 characterised in that the first valve mechanism (64) is diametrically opposite the second valve mechanism.

11. A catheter as claimed in any one of the preceding claims characterised in that the first and/or second valve mechanisms are slit valves.

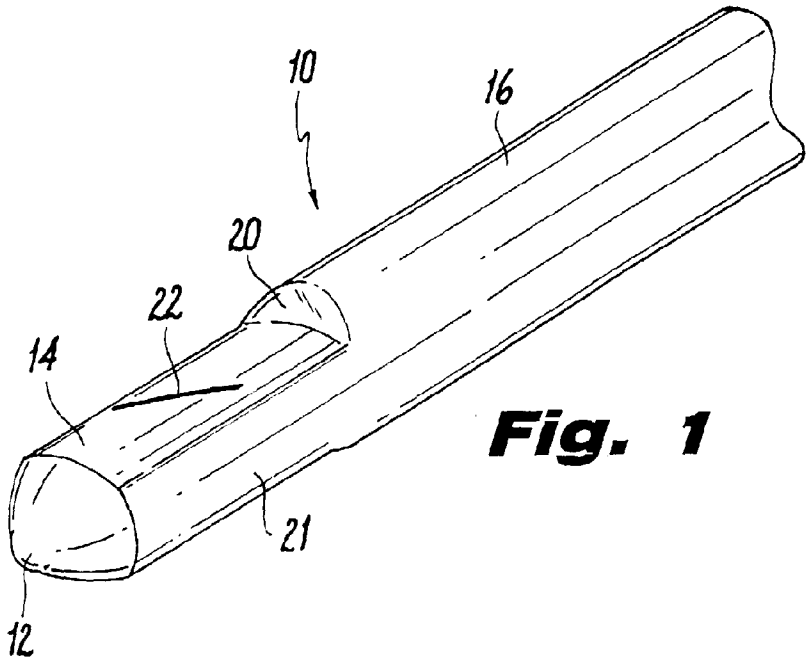

Fig. 1

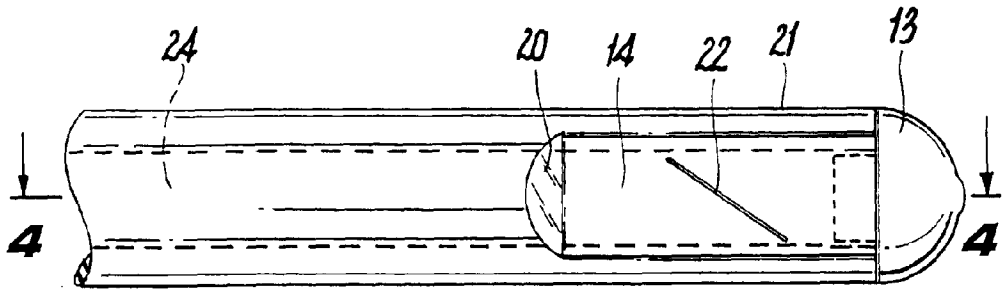

Fig. 2

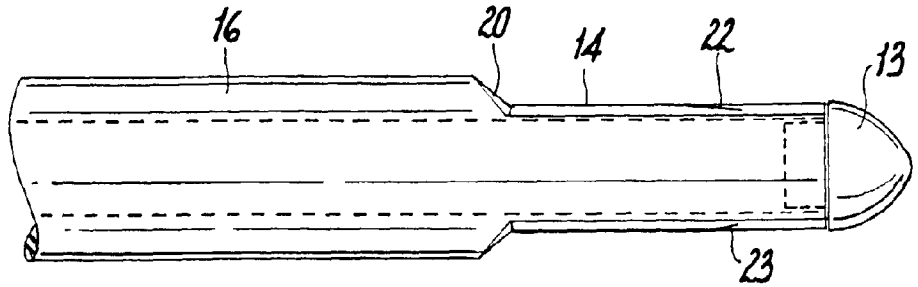

Fig. 3

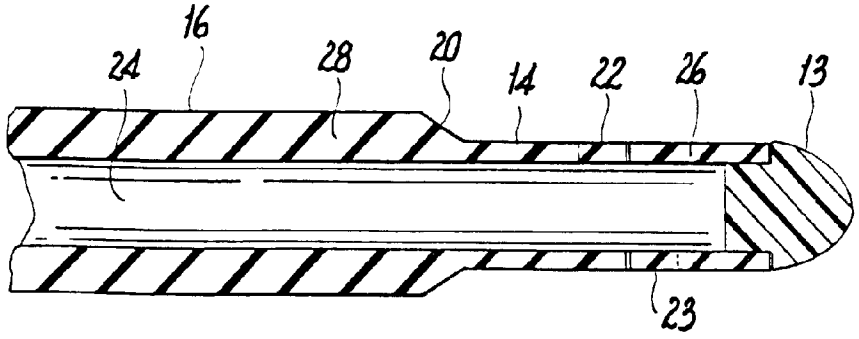

Fig. 4

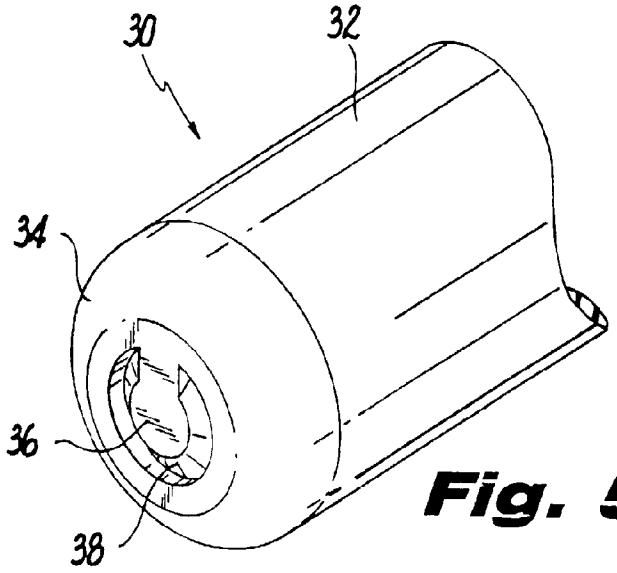

Fig. 5

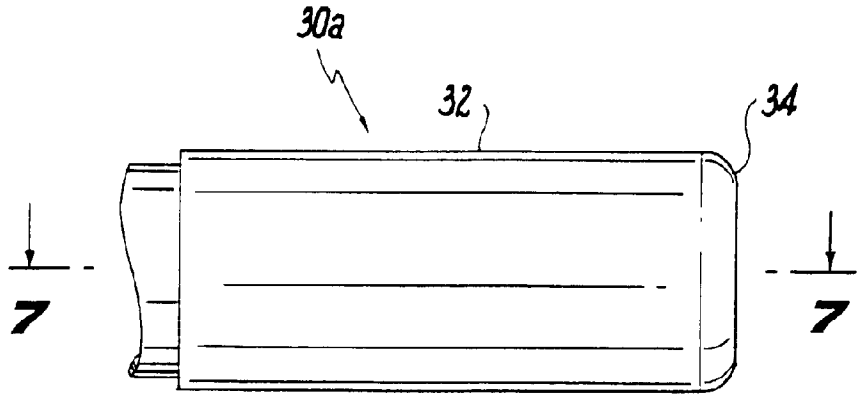

Fig. 6

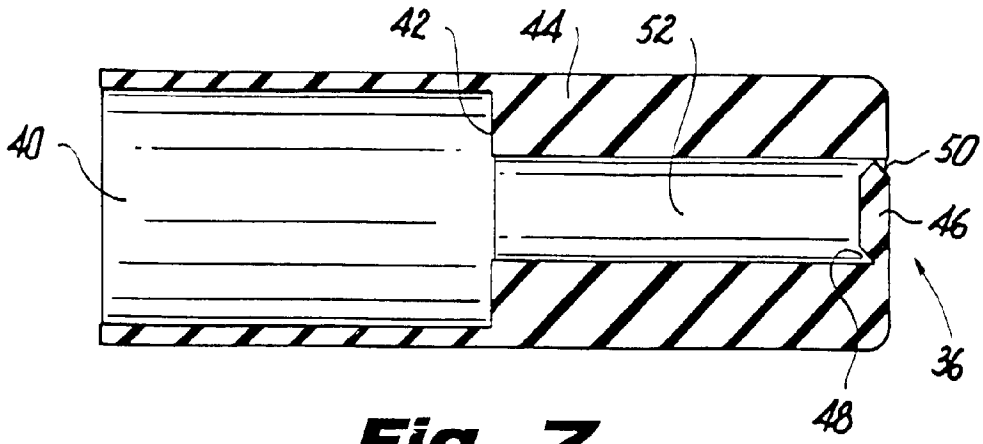

Fig. 7

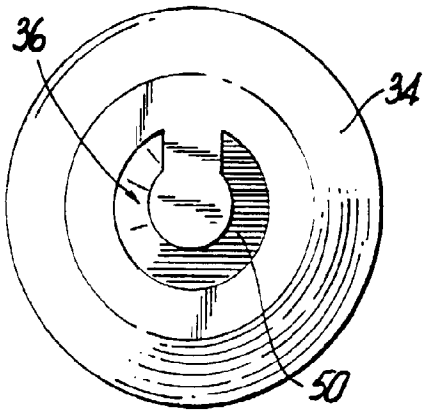

Fig. 8

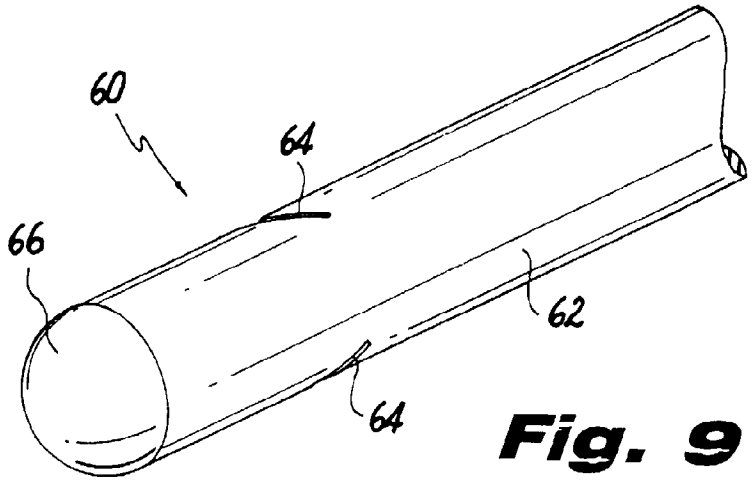

Fig. 9

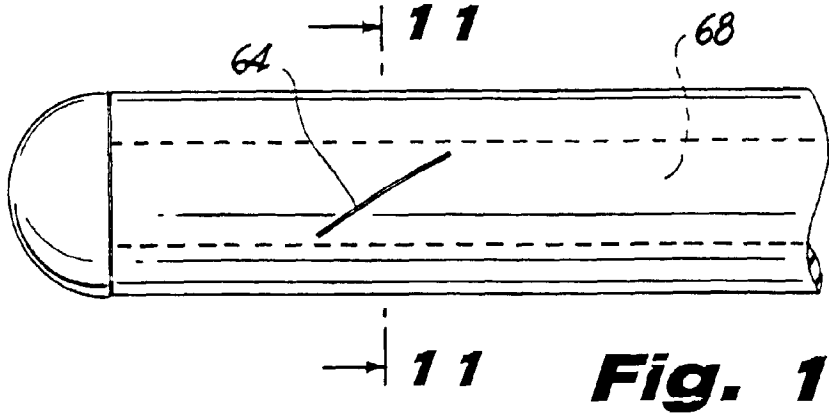

Fig. 10

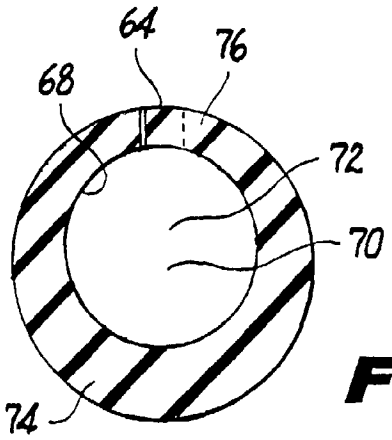

Fig. 11

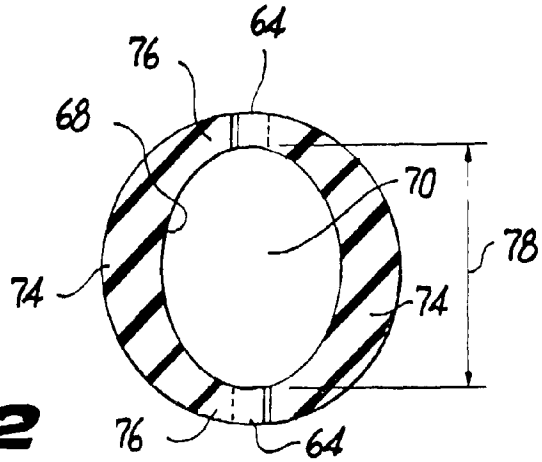

Fig. 12

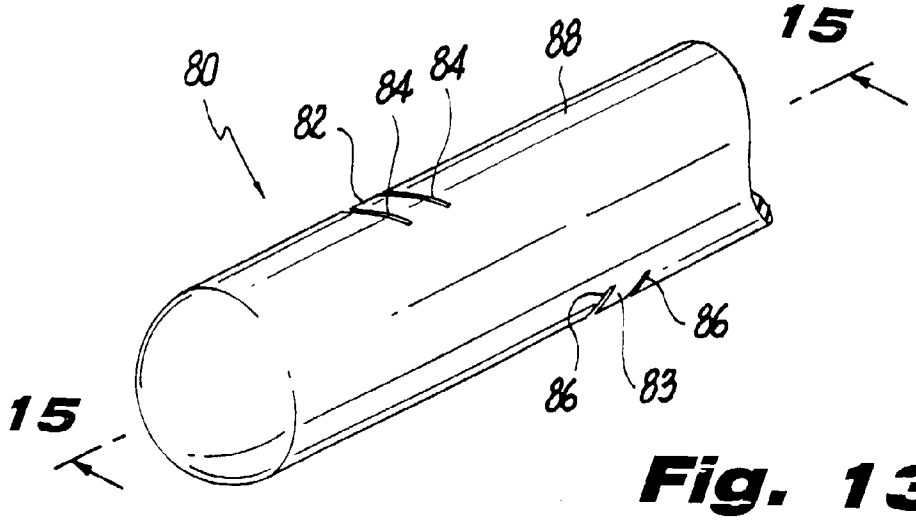

Fig. 13

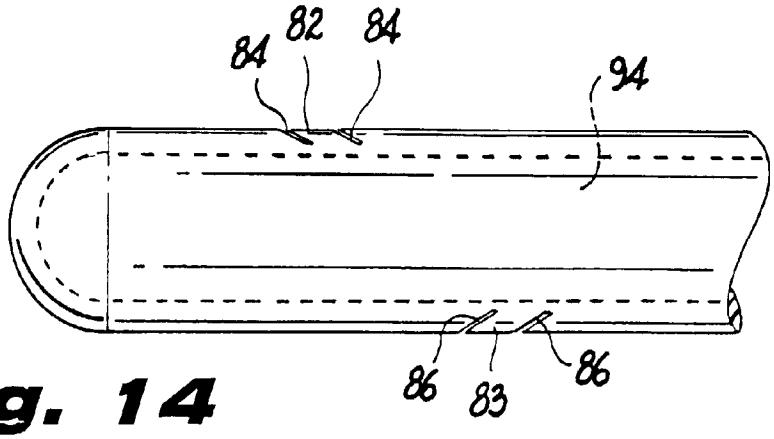

Fig. 14

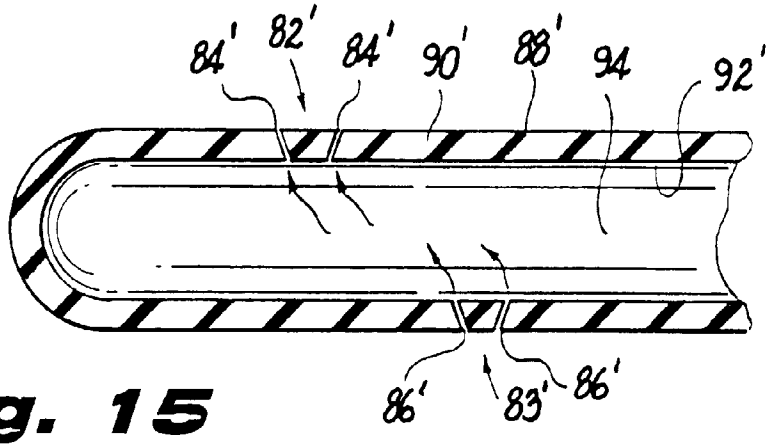

Fig. 15

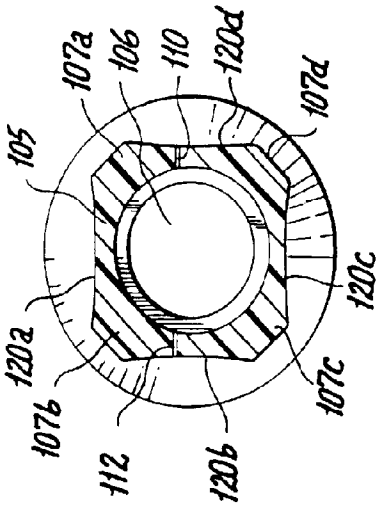

Fig. 18

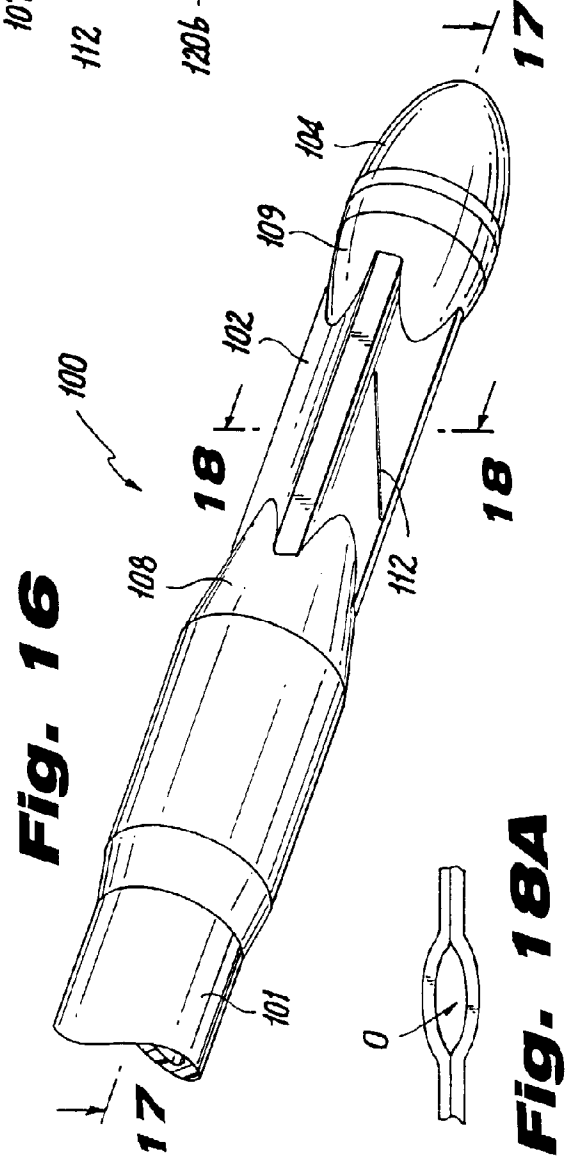

Fig. 16

Fig. 18A

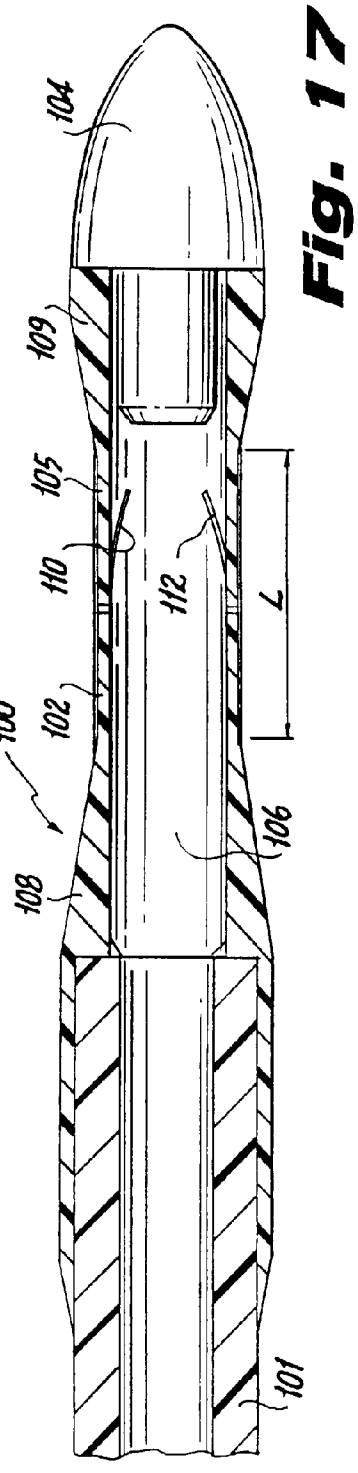

Fig. 17

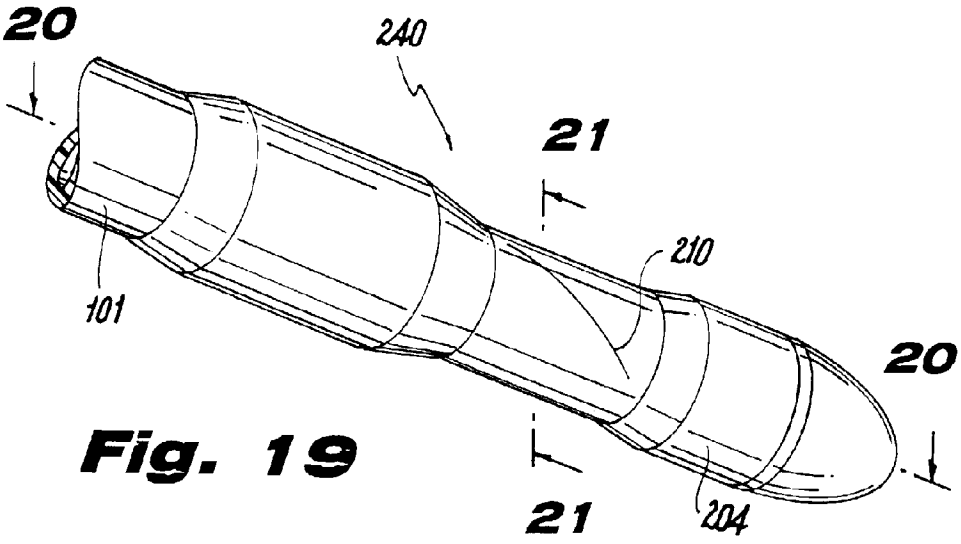

Fig. 19

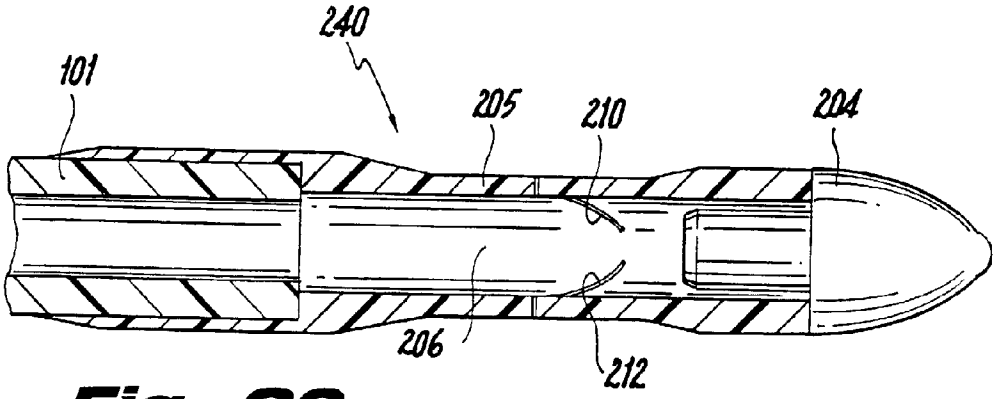

Fig. 20

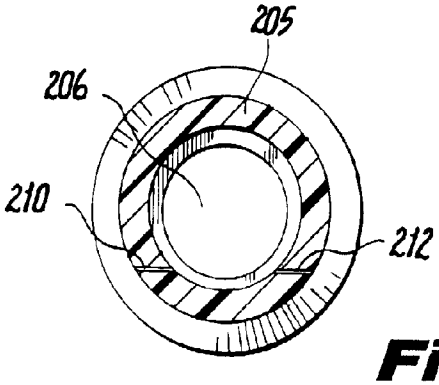

Fig. 21

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 987 042 A2

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
22.03.2000 Bulletin 2000/12

(51) Int. Cl.[7]: **A61M 25/00**, A61M 25/098

(21) Application number: **99117447.5**

(22) Date of filing: **08.09.1999**

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **15.09.1998 US 153878**
15.09.1998 US 153791
15.09.1998 US 153815
15.09.1998 US 153722
15.09.1998 US 153623
15.09.1998 US 153520
15.09.1998 US 153880

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(54) Design and method to fabricate PTCA balloon radiopaque marker band

(57) A radiopaque marker for the body portion of a medical catheter, and the methods for manufacturing such a marker, require the blending of a metal with a polymer matrix. For the blend, the metal is preferably greater than approximately seventy percent by weight. This blend is then made into a band having a thickness that is less than about two thousandths of an inch. To assemble the catheter, the radiopaque band is positioned against the catheter body and the band is then thermally bonded to the catheter body. For a balloon catheter, the catheter body will be tubular and the radiopaque marker band can be formed as a ring that will surround the catheter body, circumscribe the lumen inside the catheter body, or be incorporated as part of the catheter body. The position of the marker band can be established as desired and then thermally bonded onto the catheter body to identify the location of the balloon on the catheter body.

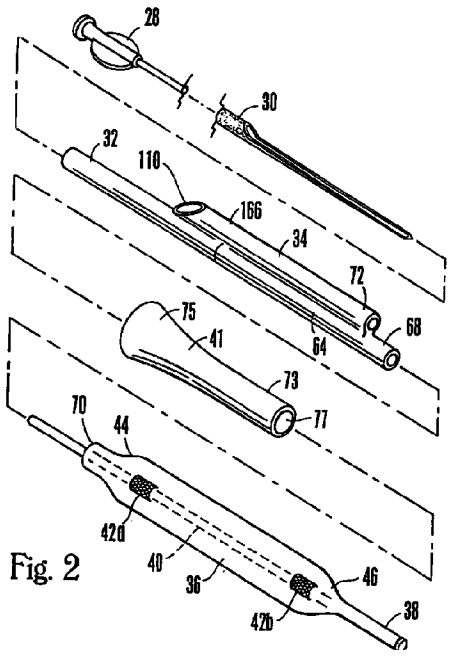

Fig. 2

EP 0 987 042 A2

Description

[0001] The present invention pertains generally to medical catheters. More particularly, the present invention pertains to the manufacture and use of radiopaque marker bands which can be positioned on a medical catheter to identify the location of the catheter during surgical procedures using fluoroscopic techniques. The present invention is particularly, but not exclusively, useful as a polymer based radiopaque marker which is flexible, and which has a low profile that will facilitate the insertion of the catheter into a body cavity.

[0002] A well known technique for precisely controlling the location of a catheter as it is being positioned in a vessel of the cardio-vascular system of a patient during angioplasty surgery is to monitor the catheter insertion using radiographic equipment. Such a procedure, however, requires that certain components of the catheter be somehow identified with radiopaque markers. Typically, the radiopaque markers which have been used for this purpose are made entirely of metal. For example, U.S. Patent 4,793,359 which issued to Sharrow for an invention entitled "Centering Balloon Structure For Transluminal Angioplasty Catheter" discloses radiopaque markers made of platinum or gold. Alternatively, U.S. Patent 5,034,005 which issued to Appling for an invention entitled "Radiopaque Marker" discloses radiopaque markers made of a surgical grade stainless steel. Although effective for the intended purpose, metal markers have their shortcomings.

[0003] Metal markers, of course, are not flexible. Flexibility, however, is a very desirable quality for an angioplasty catheter as it is necessary for improved tracking of the catheter through the coronary tree of a patient. Further, metal markers typically have rough edges and burrs which can present problems if not smoothed. For example, it is known that burrs on metal radiopaque markers are capable of causing pinholes in the balloon of an angioplasty catheter. If detected early enough, the catheter is simply not used. Unfortunately, it sometimes happens that the adverse effects caused by burrs can go unnoticed until after the catheter has been placed in use. This presents many complications which can sometimes have serious consequences. Simply stated, such consequences should be avoided if at all possible.

[0004] In addition to the shortcomings noted above, metal markers can sometimes present a restrictive profile. Generally, it is true that the wall thickness of a metal marker is added directly to the outside diameter of the catheter as it is being advanced through a vessel. One way to mitigate this increase in profile is to embed the metal markers in the catheter shaft, as disclosed in U.S. Patent Application 08/977,733, filed by Fugoso and Rowean for an invention entitled "Imbedded Marker And Flexible Guide Wire Shaft" which is assigned to the same assignee as the present invention. Another method disclosed in U.S. Patent Application 09/046,241 filed by Rafiee and Squadrito for an invention entitled "Catheter Having Extruded Radiopaque Stripes Embedded In Soft Tip And Method Of Fabrication" which is assigned to the same assignee as the present invention is to co-extrude a "radiostripe" made of a mix of molten polymer and a radiopaque powder during extrusion of the distal tip. Finally, in addition to flexibility and profile concerns, it is well known that when a completely metallic marker is to be used, it is necessary to bond or attach the marker to the angioplasty catheter using an adhesive. In general, the tasks that are required to attach a metal marker to a catheter are labor intensive and costly.

[0005] In light of the above, it is an object of the present invention to provide a marker for a medical device which has improved flexibility for tracking through the vessels of a patient's cardio-vascular system. Another object of the present invention is to provide a marker having a wall thickness of only about 0.025 mm (one thousandth of an inch) in order to present a reduced profile for an angioplasty catheter and thereby improve the catheter's ability to traverse small vessels, and lesions or stents in the vessel. Still another object of the present invention is to provide a marker for a medical device which does not present burrs or rough edges which require additional smoothing. Yet another object of the present invention is to provide a marker for a medical device which does not require the use of adhesives when affixing the marker to the device. Another object of the present invention is to provide methods for manufacturing an angioplasty balloon with radiopaque markers which are simple and easy to accomplish. Still another object of the present invention is to provide a marker for a medical device which is relatively cost effective.

[0006] A radiopaque marker for a medical device, such as a balloon angioplasty catheter, includes a polymer matrix material which is blended with a metal. For the present invention the polymer matrix material is preferably a polyether block amide co-polymer, and the metal is preferably selected from the group which includes tungsten, silver, gold, platinum and their alloys. Further, the blend should include the metal at about seventy percent, or more, by weight. An effective blend for the present invention has been a mixture of ninety percent tungsten, by weight, and a polymer which is commercially available under the trade name of Pebax®.

[0007] In accordance with the methods of the present invention, the matrix material and metal blend is first formed as a band. In particular, for its use with a balloon angioplasty catheter, the radiopaque band is formed as a ring which is dimensioned to fit around a tubular shaped catheter body, circumscribe the lumen inside the catheter body, or be incorporated as part of the catheter body. Importantly, for the present invention, the marker band and the catheter body are made of the same polymer material, or of compatible polymer materials. In this sense, compatibility means that the materi-

als should melt into each other. Regardless of which specific materials are used, once the band has been positioned as desired, it is thermally bonded to portions of the tubular catheter body using r.f. energy. To do this, an active RF mandrel is inserted through the lumen of the tubular shaped catheter body and an RF coil is positioned so that the catheter body and the marker band are located between the mandrel and the coil. A current is then applied to the coil to generate the RF energy that is needed to melt both the marker band and the catheter body. The result is an integral thermal bond between the marker band and the catheter body.

[0008] As intended for the present invention, a single marker band can be used, or a plurality of marker bands can be used and positioned anywhere on the tubular catheter body to landmark specific locations or components. Possible marker band positions include, the extreme distal tip of the catheter, the center of the balloon, brackets for stents, and guidewire entry or exit ports. Further, the radiopaque bands used for the markers need not be formed as rings. Instead, they can be formed as strips and affixed to the catheter body for similar purposes.

[0009] The novel features of this invention, as well as the invention itself, both as to its structure and its operation, will be best understood from the accompanying drawings, given by way of example only, and taken in conjunction with the accompanying description, in which similar reference characters refer to similar parts, and in which:

Fig. 1 is a perspective view of the balloon catheter of the present invention with the component subassemblies interconnected with each other;

Fig. 2 is an exploded perspective view of the catheter of the present invention showing the interconnective relationships between the component subassemblies;

Fig. 3A is a cross sectional view of the balloon subassembly of the present invention as seen along the line 3-3 in Fig. 1;

Fig. 3B is a side elevational view of the guidewire marker tube illustrating an alternative method for its assembly;

Fig. 4 is a side elevational view of the distal portion of the balloon positioned over the distal end of the guidewire-marker tube with portions broken away and shown in phantom for clarity;

Fig. 5 is an elevation cross sectional view of the balloon and guidewire-marker tube as shown in Fig. 4 and positioned in a heating die for thermally bonding the balloon to the distal end of the guidewire-marker tube;

Fig. 6 is a side elevational view of the distal tip of the catheter which results from the bonding process depicted in Fig. 5;

Fig. 7 is a perspective view of the coupling tube in a position to be joined with the proximal portion of the balloon and the distal end of dual lumen tube;

Fig. 8 is a cross sectional view of the coupling tube after it has been joined with the proximal portion of the balloon and the distal end of the dual lumen tube as would be seen along the line 8-8 in Fig. 7;

Fig. 9 is a cross sectional view of the coupling tube and guidewire marker tube as would be seen along the line 9-9 in Fig. 8 after the coupling tube has been joined with the distal end of the dual lumen tube;

Fig. 10 is a perspective view of the proximal portion of the balloon positioned for interconnection with both the proximal end of the guidewire-marker tube, and with the distal end of the dual lumen tube;

Fig. 11 is a cross sectional view of the components shown in Fig. 10 when positioned for integral bonding with each other in accordance with an alternative embodiment of the catheter of the present invention;

Fig. 12 is a cross sectional view of the catheter portion between the balloon assembly and the midsection which results from the bonding process depicted in Fig. 11;

Fig. 13 is a cross sectional view of the dual lumen tube of the present invention as would be seen along the line 13-13 in Fig. 12;

Fig. 14 is a cross sectional view of the transition "necked-down" region between the dual lumen tube and the balloon assembly as would be seen along the line 14-14 in Fig. 12;

Fig. 15A is a perspective view of the distal end of the hypotube positioned for insertion into the proximal end of the mid-tube for interconnection therewith, and the distal end of the mid-tube for interconnection with the proximal end of the dual lumen tube;

Fig. 15B is a cross sectional view of the hypotube as seen along the line 15-15 in Fig. 15A;

Fig. 16 is a cross sectional view of the distal end of the hypotube inserted for bonding with the mid-tube as would be seen along the line 16-16 in Fig. 15A;

Fig. 17 is a cross sectional view of the interconnection between the hypotube, mid-tube, and the dual lumen tube which results from the bonding process depicted in Fig. 16;

Fig. 18 is a perspective view of the catheter of the present invention shown in operative association with a guidewire and an inflator;

Fig. 19 is a schematic of the components used in the method of laminating a hypotube subassembly for use within the medical catheter of the present invention; and

Fig. 20 is a cross sectional view of the die of the extruder depicted as would be seen along the line 20-20 in Fig. 19.

[0010] Referring initially to Fig. 1, a percutaneous transluminal coronary angioplasty (PTCA) catheter

which has been manufactured in accordance with the methods of the present invention is shown and generally designated 20. In overview, the catheter 20 includes three separate and distinct subassemblies. In Fig. 1, these subassemblies are shown in their proximal-to-distal order as: a hypotube subassembly 22, a mid-section subassembly 24, and a balloon subassembly 26. As intended for the present invention, and disclosed herein, each of the subassemblies 22, 24 and 26, can be individually fabricated in separate manufacturing operations. The various subassemblies 22, 24 and 26 can then be subsequently joined together to create the catheter 20.

[0011] For the general dimensions that are presented in the final assembly of the catheter 20, it is to be appreciated that the overall length of the catheter 20 is preferably in the range of about 1350 mm ± 30 mm. Of this overall length, the hypotube subassembly 22 will be approximately one thousand and twenty millimeters (1020 mm), the mid-section subassembly 24 will be approximately three hundred millimeters (300 mm), and the balloon subassembly 26 will be approximately thirty millimeters (30 mm). However, due to the flexibility which is afforded by the separate subassembly manufacturing operations, the final product can include subassemblies 22, 24 and 26 which have been specially tailored and sized for the specific operational requirements of the catheter 20. Further, as an additional advantage of this flexibility, when a defect is detected in a pre-assembled subassembly 22, 24 or 26, only the defective subassembly needs to be discarded. Such a defect does not thereby result in a loss of the entire catheter 20.

[0012] As shown in Fig. 1, the hypotube subassembly 22 includes a luer fitting 28 and a hypotube 30 which extends distally from the luer fitting 28. For purposes of the present invention, the luer fitting 28 can be of any type well known in the pertinent art. Further, it can be made of a material that is well known in the pertinent art, such as a medical grade plastic. The hypotube 30 includes a hollow core tube which is preferably made of a stainless steel which is laminated with an external coating of a polymer. A suitable polymer for this purpose is a polyether block amide co-polymer, such as manufactured by Elf Atochem Corporation, and commercially available under the trademark Pebax®. Specifically, a suitable material for use as the laminate on hypotube 30 is Pebax® 7033. Further, the laminated polymer coating over the core tube is preferably colored blue for the purpose of visually contrasting the hypotube 30 from other components of the catheter 20. As also shown in Fig. 1, the mid-section subassembly 24 includes a mid-tube 32 which is joined to a dual lumen tube 34. In the mid-section subassembly 24, the mid-tube 32 is preferably made of a blue colored block co-polymer, such as Pebax® 7223. On the other hand, the dual lumen tube 34 is preferably made of a material which consists of about ninety percent (90%) polymer, and ten percent (10%) graphite. In this combination, Pebax 7233 is a suitable material for the polymer. This combination of polymer and graphite as used for the dual lumen tube 34 has two significant operational aspects. Firstly, the combination makes the dual lumen tube 34 black in color. Thus, for operational purposes, it is easily distinguished from other parts of the catheter 20 which are primarily blue in color. This then allows the operator to more easily identify the location of the guidewire port 110 (see Fig. 18) which will be substantially located at the margin between the mid-tube 32 and the dual lumen tube 34. Secondly, the graphite in the combination gives the dual lumen tube 34 enhanced lubricity to facilitate insertion and passage of a guidewire 118 (see Fig. 18) through the dual lumen tube 34.

[0013] The balloon subassembly 26 is shown in Fig. 1 to include a balloon 36 and a distal tip 38. Also, in phantom, it can be seen that the balloon subassembly 26 includes a guidewire-marker tube 40 which is located inside the balloon 36 and extends longitudinally along the length of the balloon 36. For the present invention, the balloon 36 is preferably made of Pebax® 7033, while the guidewire-marker tube 40 is preferably made of a blue colored Pebax® 7233. For purposes of the present invention, the balloon 36 can be manufactured in accordance with the disclosure set forth in U.S. Application Serial No. 09/002,676 for an invention entitled "Method for Making a Medical Balloon Catheter" which was filed on January 5, 1998,and which is assigned to the same assignee as the present invention. As more fully set forth below, the distal tip 38 results from the mixed melting of the balloon 36 and the guidewire-marker tube 40. Thus, for the example provided above, the distal tip 38 includes both the Pebax 7033 and Pebax 7233 polymer material.

[0014] It is to be noted at this point that the preferred polymer materials which have been selected for the fabrication of the various subassemblies 22, 24 and 26 of the catheter 20 are compatible with each other. Specifically, the selected polymer materials are compatible with each other in the sense that the Pebax® 7033, which is the preferred material used for the hypotube 30 and the balloon 36, is capable of being thermally bonded with the Pebax 7233, which is the preferred material used for the mid-tube 32, the dual lumen tube 34, the coupling tube 41, and the guidewire-marker tube 40. This is important because, as illustrated in Fig. 2, the hypotube 30 of the hypotube subassembly 22 is to be thermally bonded to the mid-tube 32 of the mid-section subassembly 24. Also, the coupling tube 41 is to be thermally bonded to the dual lumen tube 34 of the mid-section subassembly 24 and to the balloon 36 of the balloon subassembly 26. Additionally, thermal or heat bonding between the various parts of the subassemblies 22, 24 and 26 is also intended for the present invention. The skilled artisan, however, will appreciate that adhesives can be used as an alternative to thermal bonding, if appropriate.

[0015] It is to be understood that materials other than the preferred polymer materials (i.e. Pebax®) disclosed herein can be used for the assembly and manufacture of the catheter 20. For example, a Nylon 12 material that is commercially available under the trademark "VESTAMID" or a polyurethane may be suitable for the present invention. Indeed, the particular material to be used is a matter of design choice which is primarily dependent on the particular characteristics desired for the balloon. For purposes of comparison, it is to be noted that the competing characteristics for materials that are to be used for the manufacture of the catheter 20 involve a trade-off between stiffness, for column strength in the catheter body, and softness, for flexibility. On the one hand, the catheter should not be too stiff, because with increased stiffness there is also an increased susceptibility for the catheter to "kink." On the other hand, if the material is too soft, it will exhibit decreased "pushability." As a measure of the hardness of a material, durometer ratings are helpful. Larger or higher durometer readings indicate harder materials. For the materials suggested here the respective durometer ratings are: Nylon 12, 72-75 D; Pebax®, 65-72 D; and Polyurethane, 55-70 D.

[0016] It is important for the present invention that the particular polymer materials to be used will either be all the same polymer, similar polymers, or be polymers which are thermally compatible with each other. As used in the context of the present invention, thermal compatibility describes a condition wherein two mated polymer materials will bond together with no discernible interface when they are heated, i.e. they are miscible. Polymers which are identical are thermally compatible. Polymers, however, do not have to be identical to be thermally compatible.

[0017] The balloon subassembly 26 of the catheter 20 is perhaps best appreciated by cross-referencing Fig. 2 with Figs. 3A and 3B. Of particular importance in the manufacture of the balloon subassembly 26 is the presence of marker bands 42a and 42b which have been bonded with or onto the guidewire-marker tube 40. In accordance with the present invention, each of the marker bands 42a,b is formed as a ring or tube before it is bonded onto the guidewire-marker tube 40.

[0018] The range of dimensions for the marker bands 42 is important for an appreciation of how they help in providing a reduced profile for the completely assembled catheter 20. Specifically, the marker bands 42a,b can have an inner diameter which is in the range of approximately 0.575 to 0.625 mm (twenty three to twenty five thousandths of an inch) (0.023 - 0.025 inch). For any particular diameter, the wall thickness of the marker bands 42a,b can be approximately 0.05 mm (two thousandths of an inch) (0.0020 inch). Further, they will have a length which is in the range of one to two millimeters (1 - 2 mm).

[0019] As intended for the present invention, the marker bands 42a,b are preferably made of a blend of metal and polymer materials. Specifically, a Pebax® polymer, such as Pebax® 5233, can be blended with a metal selected from the group including tungsten, silver, gold, platinum, or any of the other known radiopaque metals, and their alloys. Further, in this blend, the radiopaque metal should constitute greater than approximately seventy percent of the material by weight (> 70% wt.). Preferably, for the present invention, the marker bands 42a,b include, by weight, approximately ninety percent tungsten (90% W) and approximately ten percent polymer (10% Pebax®).

[0020] Figs. 2 and 3A show that the marker bands 42a and 42b are located on the guidewire-marker tube 40 inside the balloon 36. These Figs. also show that the marker bands 42a and 42b are located, respectively, under the proximal end 44 and the distal end 46 of the balloon 36. It is to be appreciated, however, that several variations in both the location and length of the marker bands 42a,b are possible. For example, marker bands 42 can be positioned underneath the balloon 36 to landmark either the center of the balloon 36, the entire length of the balloon 36, or the lengths of various stents (not shown) which may be used with the balloon 36. Additionally, other parts of the catheter 20 can be landmarked with marker bands 42, as desired. Regardless where the marker bands 42 are to be positioned on the catheter 20, it is to be appreciated that when a compatible polymer is used for their manufacture (e.g. Pebax), the marker bands 42 can be thermally bonded to other polymer parts of the catheter 20 according to the desires of the manufacturer.

[0021] In accordance with the present invention, heat bonding of the marker bands 42 to the guidewire-marker tube 40 can be accomplished in any manner well known in the pertinent art. For example, radio frequency (RF) energy can be used to generate temperatures of around 177°C (three hundred and fifty degrees Fahrenheit) (350 F) to thermally bond the marker bands 42 to the guidewire-marker tube 40. Further, although Figs. 2 and 3A indicate that the marker bands 42a,b are positioned around the outside surface of the guidewire-marker tube 40, it is to be understood that the marker bands 42a,b could just as easily be bonded to the inside surface of the marker tube 40. In this case, the marker bands 42a,b would be inside the lumen 48 of the guidewire-marker tube 40. Alternatively, as shown in Fig. 3B, the marker bands 42a,b can be butt joint bonded into the marker tube 40. For all configurations of the marker bands 42 on tube 40, an active mandrel 45 can be used with the marker bands 42 and sections of tube 40 arranged as desired. For purposes of the present invention, active mandrels are taken to be ferrous (Fe) based materials which interact with RF energy to generate heat. This is in contrast with inactive mandrels which are made of inert materials such as gold (Au) or copper (Cu). Further, for the present invention it is preferable to use Teflon coated mandrels which will facilitate removal of the polymer from the mandrel after the bonding operation. As will be appreciated by the

skilled artisan, the dimensions and shape of a particular mandrel will determine the configuration that is taken by the polymer as it melts. This, in turn, establishes the subsequently permanent configuration of the polymer after it is cooled and removed from the mandrel.

[0022] During the manufacture of the distal tip 38, the distal tail 50, which extends from the distal end 46 of balloon 36, is positioned over the guidewire-marker tube 40 substantially as shown in Fig. 4. As shown in Fig. 5, an active radio frequency (RF) mandrel 52 is then passed through the lumen 48 of the guidewire-marker tube 40. This combination is then inserted into the cavity 54 of a mold 56. There, it is heated to a temperature in a range of approximately 99 top 177°C (two hundred and ten to three hundred and fifty degrees Fahrenheit) (210 F - 350 F). This operation melts both the Pebax material of the balloon 36 and the Pebax material of the guidewire-marker tube 40 in the mold 56. This simultaneous melting provides for an integral bonding between the balloon 36 and the guidewire-marker tube 40 in the vicinity of the distal tip 38.

[0023] Fig. 6 shows the result of the above described operation. Specifically, the resultant distal tip 38 is preferably formed by the mold 56 to have both an end taper 58 and a transition taper 60. The end taper 58, indicated by the angle α in Fig. 6, provides for a region of increasing outside diameter in the proximal direction for the distal tip 38. The angle α which is definitive of the end taper 58 is measured from the centerline 62, and can generally be in the range of about fifteen to about seventy five degrees (15 - 75). Preferably, the angle α will be around sixty degrees (α = 60). The transition taper 60, indicated by the angle β in Fig. 6, provides for another region of increasing outside diameter for the distal tip 38. This increase is also in the proximal direction. For the transition taper 60 the angle β, which is also measured from the centerline 62, will generally be in the range of about four to about six degrees (4 - 165°). Preferably the angle β will be around five degrees (β = 5).

[0024] In the assembly of the catheter 20, the midsection subassembly 24 can be connected with the balloon subassembly 26 in either of two ways. One way uses a coupling tube 41 (see Figs. 7-9). The other way does not (see Figs. 10-12). In either case, several parts of the catheter 20 need to be uniquely configured. In particular, for this purpose it will be noted in Figs. 2, 7 and 10 that the dual lumen tube 34 is formed with an inflation section 64 and a guidewire section 66. Specifically, the dual lumen tube 34 can be extruded in a manner well known in the pertinent art. Extrusion alone, however, does not suffice for the fabrication of the dual lumen tube 34. As shown in Figure 7, the inflation section 64 includes an extension 68 which projects beyond the guidewire section 66 through a distance of approximately two millimeters. Using this configuration for dual lumen tube 34, it can be seen that the proximal end 70 of the guidewire-marker tube 40 can be positioned to abut the distal end 72 of the guidewire section 66 of the dual lumen tube 34. This positioning of the guidewire-marker tube 40 against the distal end 72 of dual lumen tube 34 also brings the outer surface of the proximal end 70 of guidewire-marker tube 40 into contact with the outer surface of the extension 68 of dual lumen tube 34.

[0025] For one embodiment of the present invention, a coupling tube 41, which is approximately five centimeters (5cm) in length, is incorporated into the catheter 20. One reason this is done is to establish a greater separation between those points on the catheter 20 which react to forces created by an inflation of the balloon 36. This increased separation may be necessary because it happens that as the balloon 36 is inflated, it generates forces on the catheter 20 which tend to elongate the catheter 20. A permanent set may result from this elongation which will cause a distortion of the balloon assembly 26 after deflation of the balloon 36. Such a distortion can easily inhibit withdrawal of the catheter 20 from the patient, and should be avoided. By attaching the coupling tube 41 to one end of the balloon 36, however, the distance between points on the catheter 20 where an inflation of the balloon 36 exerts stretching forces can be effectively increased. Specifically, this increase will be by about the length of the coupling tube 41. The structure for this embodiment will be best appreciated with reference to Figs. 7 and 8.

[0026] In Fig. 7 it will be seen that the coupling tube 41 has a distal end 73 and a proximal end 75, with a lumen 77 extending through the coupling tube 41 between the ends 73, 75. Further, it is to be seen that the proximal end 75 of coupling tube 41 is flared to give the lumen 77 a larger inside diameter at the proximal end 75. This flaring can be accomplished in any manner well known in the pertinent art, such as by inserting an awl (not shown) into the lumen 77 at proximal end 75. By cross referencing Figs. 7 and 8 it will be appreciated that, in order to join the coupling tube 41 to the balloon 36, the proximal tail 74 of balloon 36 is positioned in a surrounding relationship over the distal end 73 of coupling tube 41. The proximal tail 74 is then thermally bonded to the distal end 73. To bond the coupling tube 41 to the mid-section assembly 24, the flared proximal end 75 of coupling tube 41 is positioned in a surrounding relationship over the distal end 72 of the dual lumen tube 34. Recall, the proximal end 70 of guidewire marker tube 40 also abuts the guidewire section 66 at the distal end 72 of dual lumen tube 34. The proximal end 75 of coupling tube 41 is then thermally bonded to the distal end 72 of the dual lumen tube 34. As best seen in Fig. 8, the connecting point between the proximal end 70 of guidewire marker tube 40 and the balloon 36 is effectively moved away from the balloon 36 by about the length of the coupling tube 41. As discussed above, this provides additional separation of about five centimeters (5 cm) between those points on the catheter 20 which react to the forces that are generated by an inflated balloon 36. For reasons discussed above, this is beneficial. There is, however, another benefit.

[0027] For the configuration of catheter 20 which incorporates the coupling tube 41, it can be an added benefit that the guidewire marker tube 40 is "coaxial" with the coupling tube 41. With this "coaxial" structure the flexibility of the catheter 20 is improved without degradation of the ability of catheter 20 to inflate the balloon 36. By referencing Fig. 9 it is to be appreciated that the guidewire marker tube 40 actually extends through the lumen 77 of coupling tube 41. With this relationship, the guidewire lumen 96 of dual lumen tube 34 is effectively continued through the guidewire marker tube 40. At the same time, the inflation lumen 98 of dual lumen tube 34 is placed in fluid communication with the lumen 77 of coupling tube 41, and with the interior of the balloon 36.

[0028] It is to be appreciated that the thermal bonding which is established between coupling tube 41 and the respective components of mid-section assembly 24 and balloon assembly 26 is accomplished using methods well known in the pertinent art. Essentially, these methods involve the use of active mandrels which hold and shape the polymer materials as they are heated by RF energy. As indicated throughout this disclosure, the position of mandrels, the dimensions and shape of the mandrels, and the location and activation of RF heating coils are a matter of design choice and are dictated by the desired results.

[0029] For another embodiment of the catheter 20, the connection between the mid-section assembly 24 and the balloon assembly 26 can be made without the use of a coupling tube 41 (see Figs. 10-12). With specific reference to Fig. 10, it will be appreciated that guidewire-marker tube 40 can be positioned against the dual lumen tube 34 as indicated above. Further, it is to be appreciated that the proximal tail 74 of balloon 36 can be moved into a position to surround both the distal end 72 and the extension 68 of the dual lumen tube 34. Simultaneously, the proximal tail 74 can be positioned over the proximal end 70 of guidewire-marker tube 40. With the balloon 36, guidewire-marker tube 40 and dual lumen tube 34 positioned as suggested, an active RF mandrel 76 can be sequentially inserted into the respective lumens of guidewire-marker tube 40 and the guidewire section 66 of dual lumen tube 34. At the same time, an active RF mandrel 78 can be inserted through the lumen of inflation section 64 of the dual lumen tube 34. This mandrel 78 is "active" in the sense that it heats up when exposed to RF energy. This combination is now ready for heat bonding.

[0030] To effect a bonding between the proximal tail 74 of the balloon 36, the guidewire-marker tube 40, and the dual lumen tube 34, a radio frequency (RF) coil 80 can be positioned, substantially as shown in Fig. 11. Upon activation of the coil 80, these components will bond wherever they are in contact with each other. Activation of the coil 80 actually serves two purposes. Firstly, there is the bonding action just described. Secondly, the coil 80 can be extended over at least a portion of the dual lumen tube 34 to create a "necked-down" portion 82 of the dual lumen tube 34. As best seen in Fig. 11, this necked-down portion 82 will be immediately proximal to the balloon subassembly 26 and, preferably, will be approximately four centimeters in length (4 cm.). Upon deactivation of the coil 80, the coil 80 and the two mandrels 76 and 78 are removed. The result of this bonding and "necking-down" operation is shown in Fig. 12.

[0031] As can be appreciated by cross-referencing Fig. 12 with Figs. 13 and 14, the necked-down portion 82 of dual lumen tube 34 has a smaller, more compact, cross sectional profile (Fig. 14) than does the rest of the dual lumen tube 34 (Fig. 13). The purpose for this difference in cross sectional areas is that the necked-down portion 82 is thereby able to present a slimmer profile near the balloon assembly 26. This reduced profile is particularly desirable where the catheter 20 is most likely to confront lesions or narrower vessels in the patient's vascular system.

[0032] By way of example, as shown in Fig. 13, the guidewire section 66 of dual lumen tube 34 will have an outer diameter 84 that is equal to about 0.625 mm (twenty five thousandths of an inch) (0.025 ± 0.003), and an inner diameter 86 that is equal to about 0.475 mm (nineteen thousandths of an inch) (0.019 ± 0.005). On the other hand, the inflation section 64 of dual lumen tube 34 will have an outer diameter 88 that is equal to about 0.55 mm (twenty two thousandths of an inch) (0.022 ± 0.003), and an inner diameter 90 that is equal to about 0.375 mm (fifteen thousandths of an inch) (0.015 ± 0.001). The height 92 of the dual lumen tube 34 will be approximately 1.15 mm (forty six thousandths of an inch) (0.046 ± 0.003) and the center-to-center distance 94 between the guidewire lumen 96 and the inflation lumen 98 in dual lumen tube 34 is approximately 0.55 mm (twenty two thousandths of an inch (0.022 ± 0.002)). Contrast this with the dimensions of the necked-down portion 82 shown in Fig. 14. There it will be seen that the overall outside diameter 100 of the necked-down portion 82 will be approximately 0.85 mm (thirty four thousandths of an inch) (0.034 ± 0.003). Within this configuration, the guidewire lumen 96 will have a diameter of approximately 0.425 mm (seventeen thousandths of an inch (0.017 ± 0.005)), and the inflation lumen 98 will have a diameter of approximately 0.3 mm (twelve thousandths of an inch (0.012 ± 0.005)).

[0033] The joining of the hypotube subassembly 22 with the mid-section subassembly 24 by thermal bonding is made possible by the fact that the hypotube 30 is pre-coated with a polymer. By cross referencing Figs. 15A and 15B it will be seen and appreciated that the hypotube 30 is formed with an inflation lumen 99 and is covered over its outer surface with a coating 101. Preferably, the polymer used to pre-coat the hypotube 30 is a Pebax material such as those used for other components of the catheter 20 and is approximately greater than about 0.125 to 0.25 mm (five - ten thousandths of an inch thick (0.0005 in)). More specifically, the polymer

coating is extruded onto the outer surface of the hypotube in a high speed continuous operation. For purposes of the present invention, the hypotube 30 is preferably made of stainless steel. To do this, it is to be appreciated that the hypotube 30 is straightened prior to having the polymer extruded onto its outer surface. The method whereby the hypotube subassembly 22 is manufactured for integration into the catheter 20 is noteworthy and is discussed in greater detail below. As for the configuration of the hypotube 30 used for the catheter 20 of the present invention, its structure is, perhaps, best appreciated with reference to Fig. 15A. There it will be seen that the distal end 102 of hypotube 30 has been shaved to create a skived projection 103 for this purpose. Specifically, the skived projection 103 of the distal end 102 of hypotube 30 is dimensioned for insertion into the inflation lumen 98 at the proximal end 104 of the mid-tube 32, and for subsequent heat bonding therewith. Before this is accomplished, however, the distal end 106 of mid-tube 32 will be heat bonded to the dual lumen tube 34.

[0034] In Fig. 15A it can be seen that guidewire section 66 of the dual lumen tube 34 includes a proximally oriented extension 108 which is skived or shaved to create a guidewire port 110 for the guidewire lumen 96. To be in scale with other dimensions given herein, the extension 108 will project beyond the proximal end 112 of the inflation section 64 of dual lumen 34 to a distance of about ten millimeters (10 mm). Accordingly, as the mid-tube 32 is joined with the dual lumen tube 34, the distal end 106 of mid-tube 32 will abut the proximal end 112 of inflation section 64 of the dual lumen tube 34. Also, the extension 108 of guidewire section 66 will be in contact with the outer surface of the distal end 106 of mid-tube 32.

[0035] As indicated in Fig. 16, an RF coil 114, acting in concert with an active RF mandrel (not shown), can be used to heat bond the distal end 106 of mid-tube 32 to the dual lumen tube 34. As also indicated in Fig. 16, an RF coil 116 can be similarly used to heat bond the distal end 102 of hypotube 30 to the proximal end 104 of mid-tube 32 at a point that is just proximal to the distal end 102. Importantly, with this bond, the skived projection 103 of distal end 102 extends through mid-tube 32 to a point where the extreme distal tip 113 of the hypotube 30 is slightly distal to the guidewire port 110 in order to provide some degree of stiffness for the catheter 20 in this region. Also, with this bond, the inflation lumen 99 of hypotube 30 is placed in fluid communication with the inflation lumen 98 of dual lumen tube 34.

[0036] In light of the above disclosure it is to be appreciated that the guidewire lumen 96 of catheter 20 extends distally through the catheter 20 from the guidewire port 110 in mid-section subassembly 24 to the distal tip 38 of the balloon subassembly 26. Thus, along its course, the guidewire lumen 96 passes through the guidewire section 66 of dual lumen tube 34 and through the guidewire-marker tube 40. On the other hand, the inflation lumen 98 of catheter 20 establishes fluid communication all the way from the luer fitting 28 to the balloon 36. Specifically, the inflation lumen 98 extends successively from the inflation lumen 99 of hypotube 30, through the mid-tube 32, and the inflation section 64 of dual lumen tube 34. From the dual lumen tube 34, the inflation lumen 98 empties directly through the lumen 77 of coupling tube 41 into the interior of balloon 36.

[0037] The contributions of each of the subassemblies 22, 24 and 26 to the overall functionality of the catheter 20 are noteworthy. Along the length of the catheter 20, it is the hypotube subassembly 22 which provides most of the axial strength that is necessary to give the catheter 20 good "pushability." With its different structure, the dual lumen tube 34 of mid-section subassembly 24 provides good fluid transfer properties for inflation and deflation operations of the balloon 36. At the same time, the dual lumen tube 34 allows for improved twisting and turning performance in the distal portion of the catheter 20. Specifically, due to the dual lumen design of the tube 34 there is increased resistance to potential collapsing of the inflation lumen 98 during an advancement of the catheter 20 through a patient's vascular system. The use of a coupling tube 41 provides additional separation between points on the catheter 20 which will react to an inflation of the balloon 36. This additional separation reduces the adverse consequences which can result when the catheter 20 is stretched and permanently distorted. Further, the coupling tube 41 establishes a "coaxial" arrangement between the inflation lumen 98 and the guidewire lumen 96 which benefits both the flexibility of the catheter 20 and the inflatability of the balloon 36. In the balloon subassembly 26, the marker bands 42a,b allow for good observation of the advancement of the balloon 36 and its precise position in a patient's vascular system. Further, due to the materials used in their manufacture, the marker bands 42a,b provide for enhanced flexibility of the balloon subassembly 22. Still further, due to their dimensions, the marker bands 42a,b provide a reduced and slimmer profile which allows the distal extremities of the catheter 20 to be more easily advanced farther into the patient's vascular system.

[0038] As discussed above, there must be a compatibility of materials in order for the respective hypotube, mid-section and balloon subassemblies 22, 24, 26 to be thermally bonded together. As the hypotube 30 is made of stainless steel in the preferred embodiment, in order to be bonded to the midsection subassembly 24, the hypotube 30 must be laminated with a polymer coating 101 to form the hypotube subassembly 22 of the present invention. To do this, and referring now to Fig. 19, a spool 124 of stainless steel tubing 126 is provided. The stainless steel tubing 126 is first fed into a wire straightener 128, and then into the crosshead 130 of an extruder 132. The wire straightener 128 is required because the extrusion process, wherein the polymer

coating 101 is laminated onto the hypotube 30, involves very close tolerances. More specifically, and referring briefly back to Fig. 15B, the coating 101 can have a thickness 105 in a range of substantially 0.125 to 0.25 mm (five thousandths of an inch to ten thousandths of an inch). In the preferred embodiment of the invention, a four plane wire straightener 128 is used. Once straightened, the tubing 126 is fed into the crosshead 130 of the extruder 132, in a direction as shown by arrow 133.

[0039] As shown in Fig. 19, a polymer material 138 is introduced into the hopper 140 of the extruder 132. For a detailed description of the extruder 132, refer to U.S. Patent Application Serial No. 09/108,656 for an invention entitled "Medical Devices Made By Rotating Mandrel Extrusion", which is assigned to the same assignee as the present invention. The actual lamination of polymer material 138 onto the tubing 126 is, however, perhaps best appreciated by referring to Fig. 20. Fig. 20 shows the die 134 in greater detail. In Fig. 20, it is shown that the tubing 126 passes through die bore 141 and exits from the die opening 143 of extruder 132. Specifically, the polymer material 138, which is in a molten state while in the die 134, enters through feed passageway 144, and into the extrusion chamber 145, as shown by arrows 146. As the polymer material 138 is extruded through the die opening 143 at a fixed rate, the tubing 126 is pulled through the die opening 143 of extruder 132 at a variable rate in the direction shown by arrow 148. Importantly, as the tubing 126 is pulled through the die opening 143, the polymer material 138 forms around the outer surface of the tubing 126 to create the laminated coating 101 (see Fig. 15B).

[0040] Referring back to Fig. 19, after exiting the die 134, the laminated tubing 126 is cooled as it is pulled through the water bath 135 by the puller 136. Actually, the water bath 135 cools both the tubing 126 and the coating 101, and allows the coating 101 to solidify around the tubing 126. The diameter of the laminated tubing 126 is then measured by a laser micrometer 150. This diameter reading is used by a control system 152 to maintain the thickness 105 of the coating 101 in accordance with a predetermined value as chosen by the operator, as discussed below.

[0041] It is to be appreciated by referring to Fig. 19 that, to maintain the correct thickness 105 of the coating 101, a signal 156 establishing the desired thickness 105 is used as an input for the control system 152. The laser micrometer 150 measures the actual diameter of the laminated tubing 126 and generates a micrometer output signal 154, which is sent to the control system 152. The diameter of the laminated tubing 126 can be used to manipulate the thickness 105 of the coating 101 because the stainless steel tubing diameter remains constant. With a constant stainless steel tubing diameter, any changes in diameter of the laminated tubing 126 would be due to a change in thickness 105 of the coating 101. The control system 152 then compares the desired thickness signal 156 to the output micrometer signal 154 to generate an error signal. If the error signal indicates the actual laminar coating 101 is too thin, the control system 152 sends a controller output signal 158 to the puller 136 to slow the rate at which the tubing 126 is pulled through the extruder 132. As the puller 136 slows this rate at which tubing 126 is pulled, the tubing 126 will pass through the die bore 141 more slowly. Because the tubing 126 passes through the die bore 141 more slowly and the rate of extrusion of polymer 138 is constant, the tubing 126 is exposed to the molten polymer material 138 for a longer period of time, and a thicker layer of polymer material 138 forms on the tubing 126. In this manner, the thickness 105 of the laminar coating 101 can be increased.

[0042] On the other hand, if the error signal indicates the laminar coating 101 is too thick, the control system 152, in response to a signal 154 generated by the laser micrometer 150, generates a control output signal 158 which increases the pull rate on the tubing 126. Accordingly, the tubing 126 is pulled through the die bore 141 more quickly. The result then is that less polymer material 138 coats the tubing 126 and a thinner coating 101 is obtained. The result of the method of the present invention is a tubing 126 which has a substantially uniform laminar coating 101 of a desired thickness 105 (see Fig. 15B).

[0043] After the laser micrometer 150 has verified the thickness 105 of the coating 101 is at the desired value, the tubing 126 is cut by the cutter 160 to form the laminated hypotube 30 of the present invention. After being cut, a luer fitting 28 may be attached to the hypotube 30 to form the hypotube subassembly 22 of the present invention as discussed above. The hypotube subassembly 22 is then skived and assembled within the catheter 20 as also described above.

[0044] In the operation of the catheter 20 of the present invention, and as shown in Fig. 18, a guidewire 118 is positioned in the vascular system of a patient, as desired. The proximal end 120 of guidewire 118 is then inserted into the guidewire lumen 96 at the distal tip 38 of the catheter 20. The catheter 20 is then advanced along the guidewire 118 until the proximal end 120 of guidewire 118 emerges from the guidewire port 110. By grasping the proximal end 120, the guidewire 118 can be stabilized during further advancement of the catheter 20 over the guidewire 118. This advancement continues until the balloon 36 is positioned in the vascular system of the patient, as desired. With the balloon 36 so positioned, an inflator 122, which is engaged in fluid communication with the inflation lumen 98 of luer fitting 28, is activated to inflate the balloon 36. Subsequently, the balloon 36 can be deflated and the catheter 20 withdrawn over the guidewire 118. For obvious health reasons, as intended for the present invention, the catheter 20 is to be discarded after use.

Claims

1. A radiopaque marker for locating a medical device in vivo which comprises:

   a catheter body;
   a matrix material; and
   a metal, said metal being blended into said matrix material to form a radiopaque band, said band being bonded to said catheter body to contrast therewith.

2. A medical catheter which comprises:

   a catheter body;
   a radiopaque band made of a metal blended with a matrix material, said radiopaque band being thermally bonded to said catheter; and
   a tubular shaped balloon having a first tail and a second tail, said first tail and said second tail being respectively thermal bonded to said catheter body to position at least a portion of said catheter body inside said balloon, with said radiopaque band being positioned on said catheter body to identify a location for said balloon on said catheter body.

3. A marker as recited in claim 1 or a catheter as in claim 2 wherein said matrix is made of a polyether block amide co-polymer.

4. A marker as recited in claim 1 or a catheter as in claim 2 wherein said catheter body is made of a polyether block amide co-polymer.

5. A marker as recited in claim 1 or a catheter as in claim 2 wherein said metal is selected from a group including tungsten, silver, gold, platinum and their alloys.

6. A marker or catheter as recited in claim 5 wherein said metal is at least seventy percent by weight of said radiopaque band.

7. A marker as recited in claim 1 or any claim dependent thereon, or a catheter as in claim 2 or any claim dependent thereon wherein said band is formed as a ring, said ring having an outer diameter and being formed with a lumen defined by an inner diameter.

8. A marker or catheter as recited in claim 7 wherein said outer diameter and said inner diameter have a difference therebetween to define a wall thickness, and said wall thickness is in the range of approximately (0.025 to 0.05 mm (one thousandth of an inch to two thousandths of an inch (0.001 -0.002 inch)).

9. A marker or catheter as recited in claim 8 wherein said catheter body is a tube and said band receives said catheter tube in said lumen to circumscribe at least a portion of said tube.

10. A marker or catheter as recited in claim 9 further comprising a tubular shaped balloon having a first tail and a second tail, said first tail and said second tail being respectively bonded to said catheter body to position at least a portion of said catheter body inside said balloon, with said radiopaque band being positioned on said catheter body to identify a location for said balloon on said catheter body.

11. A marker as recited in claim 1 or any claim dependent thereon, or a catheter as in claim 2 or any claim dependent thereon, further comprising a plurality of said radiopaque bands.

12. A method for thermally bonding a radiopaque marker to a catheter body which comprises the steps of:

    blending a metal with a matrix material to form a radiopaque band;
    positioning said radiopaque band against a portion of said catheter body; and
    applying RF energy to said radiopaque band and to said catheter body to thermally bond said radiopaque band to said catheter body.

13. A method as recited in claim 12 wherein said band is formed as a ring, said ring having an outer diameter and being formed with a lumen defined by an inner diameter, and wherein said catheter body is a tube, and further wherein said positioning step is accomplished by inserting at least a portion of said catheter body into said lumen of said ring.

14. A method as recited in claim 13 wherein said applying step further comprises the steps of:

    placing an active RF mandrel into said catheter body tube;
    surrounding said radiopaque marker, said catheter body tube and said mandrel with an RF coil to locate said radiopaque marker and said catheter body tube between said RF coil and said active RF mandrel; and
    sending a current through said coil.

15. A method as recited in any of claims 12 to 14 wherein said matrix material and said catheter body are made of a polyether block amide co-polymer.

16. A method as recited in any of claims 12 to 15 wherein said metal is selected from a group including tungsten, silver, gold, platinum and their alloys,

and wherein said metal is at least seventy percent by weight of said radiopaque band.

17. A method as recited in any of claims 12 to 16 wherein said catheter body further comprises a tubular shaped balloon having a first tail and a second tail, and said method further comprises the step of respectively bonding said first tail and said second tail to said catheter body to position at least a portion of said catheter body inside said balloon, with said radiopaque band being positioned on said catheter body to identify a location for said balloon on said catheter body.

18. A dual lumen tube subassembly for use in a single-operator-exchange (SOE) medical balloon catheter to interconnect the balloon with an inflator and to establish a guidewire passageway for the catheter, said subassembly comprising:

a guidewire section formed with a guidewire lumen, said guidewire section having a proximal end and a distal end;

an inflation section formed with an inflation lumen, said inflation section having a proximal end and a distal end, said inflation section being longitudinally juxtaposed with said guidewire section to create a proximal extension for said guidewire section and to create a distal extension for said inflation section;

a guidewire marker tube thermally bonded to said distal extension of said inflation section and to said guidewire section to establish a continuous guidewire passageway between said guidewire marker tube and said guidewire section; and

a mid-tube section thermally bonded to said proximal extension of said guidewire section and to said inflation section to establish a fluid passageway between said inflation section and said mid-tube section for inflating said balloon.

19. A device as recited in claim 18 wherein said guidewire section is composed of a polymer material to provide a color contrast between said guidewire section and said mid-tube section.

20. A device as recited in claim 19 wherein said polymer is a medical grade plastic.

21. A device as recited in claim 20 wherein said medical grade plastic is a polyether block amide co-polymer.

22. A device as recited in claim 21 wherein said co-polymer is Pebax.

23. A device as recited in any of claims 18 to 22 wherein said mid-tube section and said inflation section and said guidewire marker tube are made of compatible materials.

24. A device as recited in any of claims 18 to 23 wherein said proximal extension of said guidewire section is approximately ten millimeters (10 mm) long.

25. A device as recited in any of claims 18 to 24 wherein said distal extension of said inflation section is approximately two millimeters (2 mm) long.

26. A method for forming a dual lumen tube for use in a single-operator-exchange (SOE) medical balloon catheter, said dual lumen tube interconnecting the balloon with an inflator and establishing a guidewire passageway for the catheter, said method comprising the steps of:

extruding said dual lumen tube, said dual lumen tube having a proximal end and a distal end and having a guidewire section and an inflation section, said guidewire section being formed with a guidewire lumen, and said inflation section being formed with an inflation lumen, said guidewire lumen being longitudinally juxtaposed with said inflation lumen;

cutting said proximal end of said dual lumen tube to create a proximal extension for said guidewire section extending longitudinally beyond said inflation section;

cutting said distal end of said dual lumen tube to create a distal extension for said inflation section extending longitudinally beyond said guidewire section;

thermally bonding a guidewire marker tube to said distal extension of said inflation section and to said guidewire section to establish a continuous guidewire passageway between said guidewire marker tube and said guidewire section; and

thermally bonding a mid-tube section to said proximal extension of said guidewire section and to said inflation section to establish a fluid passageway between said inflation section and said mid-tube section for inflating said balloon.

27. A method as recited in claim 26 wherein said dual lumen tube is made of a material of a polymer material which provides a color contrast between said guidewire section and said mid-tube section.

28. A method as recited in claim 26 to 27 further comprising the step of skiving said proximal extension of said guidewire section prior to said thermal bonding of said mid-tube section to said inflation section and to said extension of said guidewire section.

29. A method as recited in claim 26, 27 or 28 wherein said thermal bonding is accomplished using radio frequency (RF) energy.

30. A method as recited in any of claims 26 to 29 wherein said thermal bonding is accomplished at substantially 177°C (three hundred and fifty degrees Fahrenheit (350 F)).

31. A method as recited in any of claims 26 to 30 wherein said cutting of said proximal end is accomplished to make said proximal extension of said guidewire section approximately ten millimeters (10 mm) long.

32. A method as recited in any of claims 26 to 31 wherein said cutting of said distal end is accomplished to make said distal extension of said inflation section approximately two millimeters (2 mm) long.

33. A hypotube subassembly for establishing an inflation airway for a medical balloon catheter which comprises:

a hypotube having an outer surface, a proximal end, and a distal end, said distal end being shaved to form a skived projection;
a coating positioned over said outer surface of said hypotube; and
a mid-tube having a proximal end and a distal end, said mid-tube being formed with a lumen for receiving said skived projection of said hypotube therein with said proximal end of said mid-tube being bonded to said coating on said hypotube proximal to said distal end of said hypotube and said distal end of said mid-tube being connected to said balloon to establish said airway through said hypotube to said balloon.

34. A hypotube subassembly as recited in claim 33 wherein said skived projection extends substantially through said mid-tube.

35. A hypotube subassembly as recited in claim 33 or 34 wherein said coating is made of a polymer material and said mid-tube is made of a polymer material.

36. A hypotube subassembly as recited in claim 35 wherein said polymer material of said coating and said polymer material of said mid-tube are polyether block amid co-polymers.

37. A hypotube subassembly as recited in claim 36 wherein said polymer material of said coating is a Pebax 7030 and said polymer material of said mid-tube is a Pebax 7233.

38. A hypotube subassembly as recited in any of claims 33 to 37 wherein said hypotube is approximately one meter in length, said skived projection of said hypotube is approximately fifty five mm in length, and said mid-tube is approximately sixty mm in length.

39. A hypotube subassembly as recited in any of claims 33 to 38 further comprising a luer fitting connected to said proximal end of said hypotube.

40. A hypotube subassembly defining a longitudinal axis and formed with a lumen extending along said axis for establishing an inflation airway for a medical balloon catheter between an inflator and a balloon, said hypotube subassembly comprising:

a first section having a wall surrounding said lumen, said wall of said first section including a reinforcement completely surrounding said lumen to establish a longitudinal stiffness for said hypotube subassembly in said first section, said reinforcement having a skived projection extending therefrom; and
a second section extending longitudinally from said first section and having a wall surrounding both said lumen and said skived extension of said reinforcement to reduce the longitudinal stiffness in said second section, relative to said first section, and establish increased flexibility for said second section, relative to said first section.

41. A hypotube subassembly as recited in claim 40 wherein said reinforcement is a hypotube.

42. A hypotube subassembly as recited in claim 40 or 41 wherein said skived projection extends substantially through said second section.

43. A hypotube subassembly as recited in claim 40, 41 or 42 wherein said reinforcement has an outer surface wherein said wall of said first section includes a coating of polymer material positioned over said outer surface of said reinforcement, and further wherein said wall of said second section is a polymer material.

44. A hypotube subassembly as recited in claim 43 wherein said polymer material of said coating and said polymer material of said second section are polyether block amid co-polymers.

45. A hypotube subassembly as recited in claim 44 wherein said polymer material of said coating is a Pebax 7030 and said polymer material of said mid-

tube is a Pebax 7233.

46. A hypotube subassembly as recited in any of claims 40 to 45 wherein said first section Is approximately one meter in length, said skived projection of said reinforcement is approximately fifty five mm in length, and said section is approximately sixty mm in length.

47. A hypotube subassembly as recited in any of claims 40 to 46 further comprising a luer fitting connected to said first section with said first section being located between said luer fitting and said second section.

48. A device for providing an air passageway to inflate a balloon of a medical balloon catheter and for providing stiffness to increase pushability of said medical balloon catheter which comprises:

a metal hypotube having a distal end, a proximal end and an outer surface;
a skived projection extending distally from said distal end of said metal hypotube;
a polymer coating attached to said outer surface;
a polymer mid-tube formed with a lumen for receiving said skived projection therein to place said hypotube in fluid communication with said mid-tube, said polymer mid-tube being thermally bonded to said coating to position and hold said skived projection in said lumen of said polymer mid-tube; and
means for connecting said polymer mid-tube in fluid communication with said balloon to inflate said balloon through said hypotube.

49. A device as recited in claim 48 wherein said skived projection extends substantially through said mid-tube, and wherein said coating and said mid-tube are made of a polymer material.

50. A device as recited in claim 49 wherein said polymer material of said coating and said polymer material of said mid-tube are polyether block amid co-polymers.

51. A device as recited in claim 50 wherein said polymer material of said coating is a Pebax 7030 and said polymer material of said mid-tube is a Pebax 7233.

52. A device as recited in any of claims 48 to 51 wherein said hypotube is approximately one meter in length, said skived projection is approximately fifty five mm in length, and said mid-tube is approximately sixty mm in length, and wherein said device further comprises a luer fitting connected to said proximal end of said hypotube.

53. An inflatable balloon subassembly for a medical catheter which comprises:

an inflatable balloon having a proximal tail and a distal tail;
a guidewire tube having a proximal end and a distal end, said distal tail of said balloon being connected to said distal end of said guidewire tube in a surrounding relationship thereto; and
a catheter body formed with a guidewire lumen and an inflation lumen, said proximal end of said guidewire tube being connected to said catheter body in fluid communication with said guidewire lumen thereof to establish a passageway for receiving a guidewire therethrough, and said proximal tail of said balloon being connected to said catheter body to establish fluid communication between said balloon and said inflation lumen of said catheter body.

54. A balloon subassembly as recited in claim 53 further comprising a coupling tube formed with a lumen and having a proximal end and a distal end, said proximal tail of said balloon being connected to said distal end of said guidewire tube in a surrounding relationship thereto, and said proximal end of said coupling tube being connected to said catheter body.

55. A balloon subassembly as recited in claim 54 wherein said balloon, said guidewire tube, said catheter body and said coupling tube are made of compatible polymers.

56. A balloon subassembly as recited in claim 54 or 55 wherein said coupling tube is approximately five centimeters in length (5 cm).

57. A balloon subassembly as recited in claim 54, 55 or 56 wherein said guidewire lumen and said inflation lumen of said catheter body are longitudinally juxtaposed.

58. A balloon subassembly as recited in any of claims 53 to 57 wherein said coupling tube and said guidewire tube are coaxial.

59. A balloon subassembly as recited in any of claims 53 to 58 wherein said balloon is thermally bonded to said guidewire tube, said guidewire tube is thermally bonded to said catheter body, and said coupling tube is thermally bonded to said balloon and thermally bonded to said catheter body.

60. An inflatable balloon subassembly for a medical

catheter which comprises:

a dual lumen tube having a first lumen and a second lumen;
a single lumen tube connected in fluid communication with said first lumen of said dual lumen tube to establish a passageway for receiving a guidewire therethrough;
a coupling tube having a lumen for receiving said single lumen tube therethrough, said coupling tube being connected to said dual lumen tube in fluid communication with said second lumen thereof; and
a balloon having a distal tail and a proximal tail, said distal tail of said balloon being connected to said single lumen tube in a surrounding relationship thereto and said proximal tail of said balloon being connected to said coupling tube in fluid communication therewith.

61. A balloon subassembly as recited in claim 60 wherein said coupling tube is approximately five centimeters in length (5 cm).

62. A balloon subassembly as recited in claim 60 or 61 wherein said first lumen and said second lumen of said dual lumen tube are longitudinally juxtaposed, and wherein said coupling tube and said single lumen tube are coaxial.

63. A balloon subassembly as recited in claim 60, 61^or 62 wherein said balloon is thermally bonded to said single lumen tube, said single lumen tube is thermally bonded to said dual lumen tube, and said coupling tube is thermally bonded to said balloon and thermally bonded to said dual lumen tube.

64. A balloon subassembly as recited in any of claims 60 to 63 wherein said balloon, said single lumen tube, said dual lumen tube and said coupling tube are made of compatible polymers.

65. A balloon subassembly as recited in claim 64 wherein said polymer is Pebax.

66. A method for manufacturing an inflatable balloon subassembly for a medical catheter which comprises the steps of:

providing a tubular shaped balloon having a distal tail and a proximal tail, a guidewire tube formed with a lumen and having a distal end and a proximal end, a coupling tube formed with a lumen and having a distal end and a proximal end, and a dual lumen tube formed with a first lumen and a second lumen;
thermally bonding said distal tail of said balloon to said distal end of said guidewire tube in a surrounding relationship therewith;
thermally bonding said proximal end of said guidewire tube in fluid communication with said first lumen dual lumen tube to establish a passageway for receiving a guidewire therethrough;
thermally bonding said proximal end of said coupling tube to said dual lumen tube to surround said guidewire tube and to establish fluid communication between said lumen of said coupling tube and said second lumen of said dual lumen tube; and
thermally bonding said proximal tail of said balloon to said distal end of said coupling tube to establish fluid communication therebetween.

67. A method as recited in claim 66 wherein said balloon, said guidewire tube, said dual lumen tube and said coupling tube are made of compatible polymers.

68. A method as recited in claim 66 or 67 wherein said coupling tube is approximately five centimeters in length (5 cm).

69. A method as recited in claim 66, 67 or 68 wherein said first lumen and said second lumen of said dual lumen tube are longitudinally juxtaposed.

70. A method as recited in any of claims 66 to 69 wherein said coupling tube and said guidewire tube are coaxial.

71. A method for manufacturing a medical balloon catheter having a hypotube subassembly for use in interconnecting the balloon of the catheter with an inflator, comprising the steps of:

providing a source of metal tubing, said tubing having an outer surface;
straightening said tubing;
pulling said tubing at a variable rate through a die opening of an extruder in response to a control signal;
extruding a polymer material through said die opening to form a laminar coating of said polymer material on said outer surface of said tubing as said tubing is pulled through said die opening, said coating having a thickness;
cooling said tubing and said coating;
measuring said thickness of said coating to generate said control signal for said pulling step to maintain a substantially uniform thickness for said coating
cutting said tubing and said coating to form a laminated tube, said tube having a length with a proximal end and a distal end;
fixing a luer hub fitting to said proximal end of

said tube;

engaging said inflator with said luer hub fitting to establish fluid communication between said inflator and said proximal end of said tube; and attaching an inflatable balloon in fluid communication with said distal end of said tube.

72. A method as recited in claim 71 wherein said source of metal tubing is a spool of stainless steel tubing.

73. A method as recited in claim 71 or 72 wherein said straightening step is accomplished with a four plane wire straightener.

74. A method as recited in claim 71, 72 or 73 wherein said rate of said pulling step is approximately 15 m per minute (fifty feet per minute (50 ft/min)).

75. A method as recited in any of claims 71 to 74 wherein said laminar coating is a polymer material made of a medical grade plastic.

76. A method as recited in claim 75 wherein said medical grade plastic is a polyether block amide co-polymer.

77. A method as recited in claim 76 wherein said co-polymer is Pebax.

78. A method as recited in any of claims 71 to 78 wherein said coating is colored blue to contrast said hypotube subassembly within said catheter.

79. A method as recited in any of claims 71 to 78 wherein said measuring step is accomplished with a laser micrometer, said micrometer having a control system for generating said control signal for said pulling step.

80. A method as recited in any of claims 71 to 79 wherein said attaching step is accomplished with thermal bonding.

81. A method as recited in claim 80 wherein said thermal bonding is accomplished using radiofrequency (RF) energy at approximately 177°C (three hundred and fifty degrees Fahrenheit (350 F)).

82. A method as recited in any of claims 71 to 81, further comprising the step of:

skiving said distal end of said tube, said skiving step to be accomplished after said fixing step and before said attaching step.

83. A medical balloon catheter having a hypotube subassembly for interconnecting the balloon with an inflator, comprising:

a metal tube having an outer surface, a proximal end and a distal end;
a polymer coating laminated onto said outer surface of said tube, said coating being laminated on said outer surface by passing said tube through a die bore of an extruder and extruding a polymer material through said die bore onto said surface to obtain a substantially uniform thickness for said coating on said tube;
a luer fitting bonded to said polymer coating at said proximal end of said tube, said luer fitting being engageable with an inflator; and
an inflatable balloon subassembly bonded to said polymer coating at said distal end of said tube to place said inflator in fluid communication with said balloon.

84. A device as recited in claim 83 wherein said thickness of said coating is measured to generate a control signal and said tube is passed through said die bore at a rate responsive to said control signal.

85. A device as recited in claim 83 or 84 wherein said polymer material is a medical grade plastic and said metal tube is made of stainless steel.

86. A device as recited in claim 85 wherein said medical grade plastic is a polyether block amide co-polymer.

87. A device as recited in claim 86 wherein said co-polymer is Pebax.

88. A device as recited in any of claims 83 to 87 wherein said tube is approximately one thousand and twenty millimeters (1020 mm) in length.

89. A device as recited in any of claims 83 to 88 wherein said coating is colored blue, for the purpose of contrasting said hypotube subassembly within said catheter.

90. A distal tip for advancing a medical catheter over a guidewire which comprises:

a tubular shaped balloon having a proximal tail and a distal tail, said balloon being made of a first polymer; and
a tube for receiving the guidewire therethrough, said tube having a proximal end and a distal end, said tube being made of a second polymer, said distal end of said tube being affixed to said distal tail of said balloon to establish an integral bond therebetween.

91. A distal tip as recited in claim 90 wherein both said

first polymer and said second polymer are a polyether block amide co-polymer.

92. A distal tip as recited in claim 90 or 91 wherein said first polymer and said second polymer are made of the same material.

93. A distal tip as recited in claim 90, 91 or 92 wherein both said first polymer and said second polymer are miscible with each other.

94. A distal tip as recited in claim 90, 91 or 92 wherein said distal tip is formed with an end taper and a transition taper, said transition taper being proximal to said end taper and contiguous therewith, and wherein both said end taper and said transition taper have an increasing diameter in the proximal direction:

95. A distal tip as recited in claim 94 wherein said tube defines a longitudinal axis and said end taper is characterized by an angle α which is measured from the longitudinal axis of said tube and is in the range of from about fifteen degrees to about seventy-five degrees (α = 15 - 75).

96. A distal tip as recited in claim 94 wherein said tube defines a longitudinal axis and said transition taper is characterized by an angle β which is measured from the longitudinal axis of said tube and is in the range of from about four degrees to about ten degrees (β = 4° - 10°).

97. A distal tip as recited in any of claims 90 to 96 wherein said tube is formed with a lumen for receiving a guidewire therethrough.

98. A distal tip for a medical catheter which comprises:

an end taper; and
a transition taper, said transition taper being proximal to said end taper and contiguous therewith, and wherein both said distal taper and said transition taper have an increasing diameter in the proximal direction.

99. A distal tip as recited in claim 98 wherein said medical catheter comprises:

a tubular balloon having a proximal end and a distal end with said distal end being integrally bonded to said tip; and
a tube having a proximal end and a distal end, said tube being positioned inside said balloon with said distal end of said tube integrally bonded to said balloon and to said tip.

100. A distal tip as recited in claim 99 wherein said tube defines a longitudinal axis and said end taper is characterized by an angle α which is measured from the longitudinal axis of said tube and is in the range of from about fifteen degrees to about seventy-five degrees (α = 15 - 75).

101. A distal tip as recited in claim 100 wherein said transition taper is characterized by an angle β which is measured from the longitudinal axis of said tube and is in the range of from about four degrees to about ten degrees (β = 4° - 10°).

102. A distal tip as recited in claim 99 wherein said balloon is made of a first polymer, said tube is made of a second polymer, and said tip is made of a melt combination of said first polymer and said second polymer.

103. A distal tip wherein said first polymer and said second polymer are the same polymer.

104. A method for manufacturing the distal tip of an angioplasty balloon catheter which comprises the steps of:

providing a tube having a proximal end and a distal end with a lumen formed through said tube therebetween, said tube being made of a first polymer;
inserting a mandrel into said lumen of said tube;
positioning a tubular balloon having a proximal tail and a distal tail to surround said tube and to place said distal tail of said balloon over said distal end of said tube, said tubular balloon being made of a second polymer;
introducing said distal end of said tube with said distal tail of said balloon into a cavity mold to hold said distal end of said tube and said distal tail of said balloon between said mold and said mandrel; and
energizing said mold to melt said first polymer of said distal end of said tube and said second polymer of said distal tail of said balloon to establish an integral bond therebetween.

105. A method as recited in claim 104 wherein said mandrel is an active RF mandrel.

106. A method as recited in claim 104 or 105 wherein both said first polymer and said second polymer are a polyether block amide co-polymer.

107. A method as recited in claim 104 or 105 wherein said first polymer and said second polymer are made of the same material.

108. A method as recited in claim 104 or 105 wherein

both said first polymer and said second polymer are miscible with each other.

109. A method as recited in any of claims 104 to 108 wherein said energizing step forms said distal tip with an end taper and a transition taper, said transition taper being proximal to said end taper and contiguous therewith, and wherein both said distal taper and said transition taper have an increasing diameter in the proximal direction and wherein said tube defines a longitudinal axis and said end taper is characterized by an angle α which is measured from the longitudinal axis of said tube and is in the range of from about fifteen degrees to about seventy-five degrees (α = 15 - 75), and further wherein said transition taper is characterized by an angle β which is measured from the longitudinal axis of said tube and is in the range of from about four degrees to about ten degrees (β = 4° - 10°).

110. A medical catheter which comprises:

a hypotube subassembly including a core tube, said core tube being formed with an inflation lumen extending therethrough;

a mid-section subassembly having a proximal end and a distal end, said mid-section subassembly having a guidewire lumen longitudinally juxtaposed with an inflation lumen, said proximal end of said mid-section subassembly being thermally bonded with said hypotube subassembly to connect said inflation lumen of said core tube in fluid communication with said inflation lumen of said mid-section subassembly; and

a balloon subassembly including a balloon having a proximal tail and a distal tail and a guidewire tube having a proximal end and a distal end, said distal tail of said balloon being attached to said guidewire tube proximal said distal end of said guidewire tube, and said proximal tail of said balloon being thermally bonded to said distal end of said mid-section subassembly to interconnect said guidewire tube with said guidewire lumen of said mid-section subassembly and to connect said balloon in fluid communication with said inflation lumen of said mid-section subassembly.

111. A catheter as recited in claim 110 wherein said mid-section subassembly is made of a polymer material and said hypotube subassembly further comprises a polymer coating on said core tube for thermally bonding said mid-section subassembly to said coating of said hypotube subassembly.

112. A catheter as recited in claim 110 further comprising a coupling tube having a proximal end and a distal end, said distal end of said coupling tube being connected with said proximal tail of said balloon and said proximal end of said coupling tube being connected to said distal end of said mid-section subassembly.

113. A catheter as recited in claim 112 wherein said coupling tube is approximately five centimeters in length and is made of a polymer material for thermally bonding said coupling tube to said mid-section subassembly.

114. A catheter as recited in any of claims 110 to 113, wherein said hypotube subassembly is selected from a plurality of substantially similar hypotube subassemblies prior to being thermally bonded to said mid-section subassembly.

115. A catheter as recited in any of claims 110 to 114, wherein said mid-section subassembly is selected from a plurality of substantially similar mid-section subassemblies prior to being thermally bonded to said hypotube subassembly and prior to being thermally bonded to said balloon subassembly.

116. A catheter as recited in any of claims 110 to 115, wherein said balloon subassembly is selected from a plurality of substantially similar balloon subassemblies prior to being thermally bonded to said mid-section subassembly.

117. A catheter as recited in any of claims 110 to 116, wherein said coating of said hypotube subassembly, said mid-section subassembly and said balloon subassembly are made of compatible materials.

118. A catheter as recited in claim 111 wherein said hollow core tube is made of stainless steel and said surrounding coating is a medical grade plastic.

119. A catheter as recited in claim 118 wherein said medical grade plastic is a polyether block amide copolymer.

120. A catheter as recited in claim 119 wherein said medical grade plastic coating is colored for the purpose of visually contrasting said hypotube sub assembly within said catheter.

121. A catheter as recited in any of claims 110 to 120 wherein said thermal bonding is accomplished by the use of radio frequency (RF) energy.

122. A catheter as recited in claim 121 wherein said thermal bonding is accomplished at approximately 177°C (350 degrees Fahrenheit (350 °F)).

123. A catheter as recited in any of claims 110 to 122

wherein said hypotube subassembly is approximately one thousand and twenty millimeters (1020 mm) in length.

124. A catheter as recited in any of claims 110 to 123 wherein said mid-section subassembly is approximately three hundred millimeters (300 mm) in length.

125. A method for manufacturing a catheter comprising the steps of:

manufacturing a plurality of hypotube subassemblies, each said hypotube subassembly including a core tube, said core tube being formed with an inflation lumen extending therethrough;
constructing a plurality of a mid-section subassemblies, each said mid-section having a guidewire lumen longitudinally juxtaposed with an inflation lumen;
fabricating a plurality of balloon subassemblies, each said balloon subassembly including a balloon having a proximal tail and a distal tail and a guidewire tube having a proximal end and a distal end and a coupling tube having a proximal end and a distal end, said distal tail of said balloon being attached to said guidewire tube proximal said distal end of said guidewire tube, and said distal end of said coupling tube being attached to said proximal end of said balloon;
selecting one hypotube subassembly from said plurality of hypotube subassemblies;
selecting one mid-section subassembly from said plurality of mid-section subassemblies;
selecting one balloon subassembly from said plurality of balloon subassemblies;
thermally bonding said hypotube subassembly to said proximal end of said selected mid-section subassembly to place said inflation lumen of said core tube in fluid communication with said inflation lumen of said mid-section subassembly; and
thermally bonding said proximal end of said coupling tube to said distal end of said mid-section subassembly to interconnect said guidewire tube with said guidewire lumen of said mid-section subassembly, and to connect said balloon in fluid communication with said inflation lumen of said mid-section subassembly.

126. A method as recited in claim 125 wherein said thermal bonding is accomplished using radio frequency (RF) energy.

127. A method as recited in claim 125 or 126, wherein said thermal bonding is accomplished at approximately 177°C (three hundred fifty degrees Fahrenheit (350° F)).

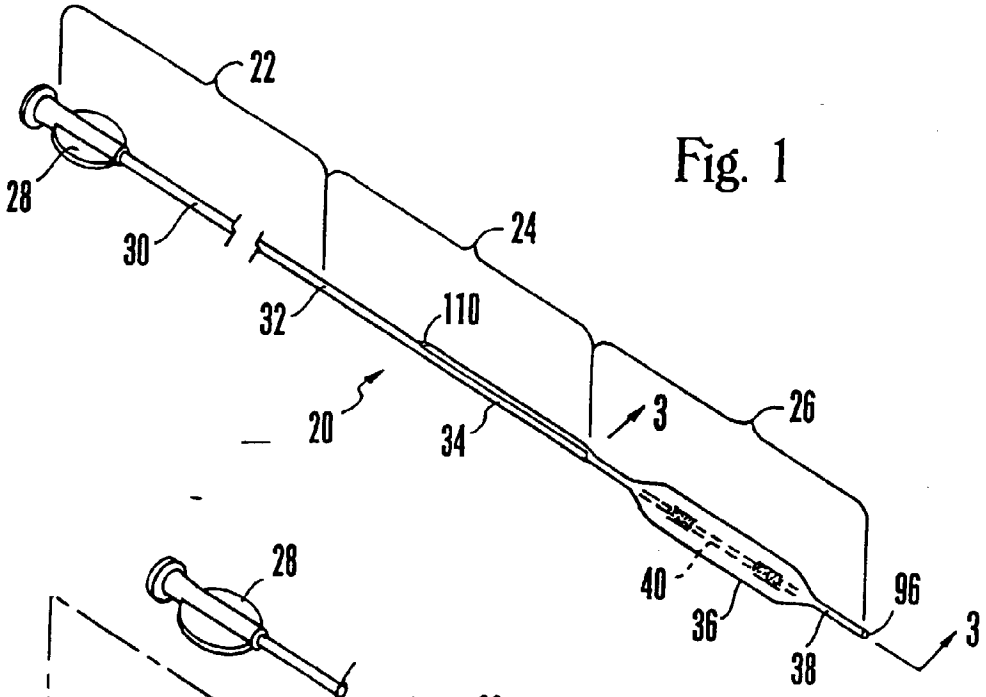
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Fig. 1

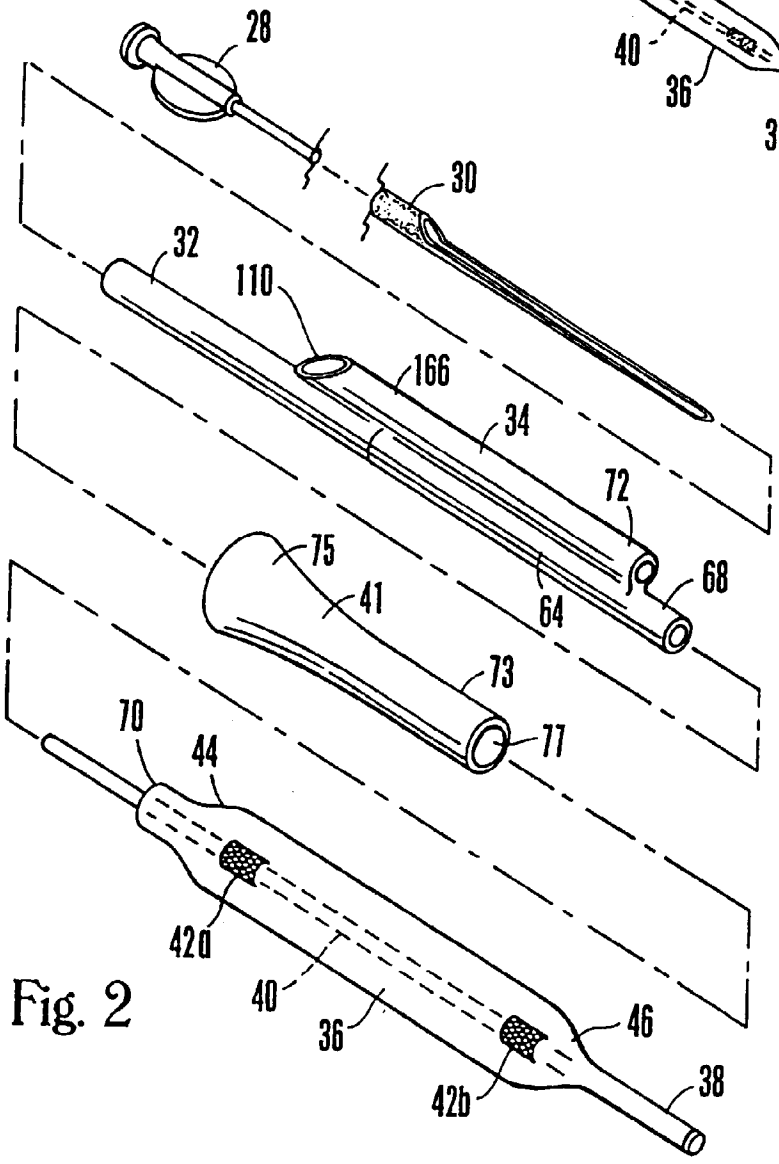
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Fig. 2

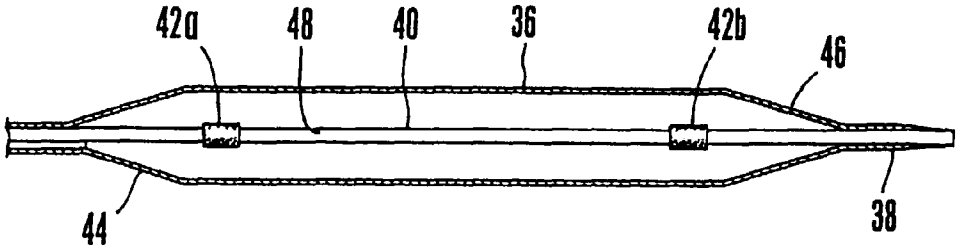


Fig. 3A

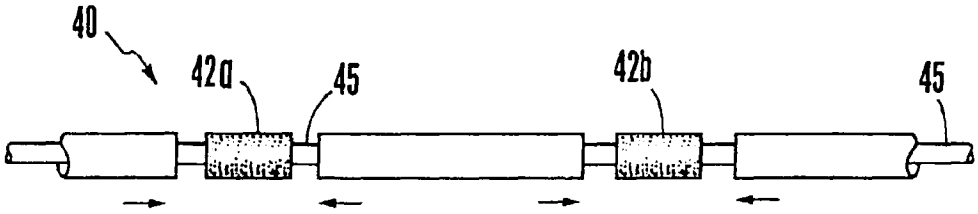
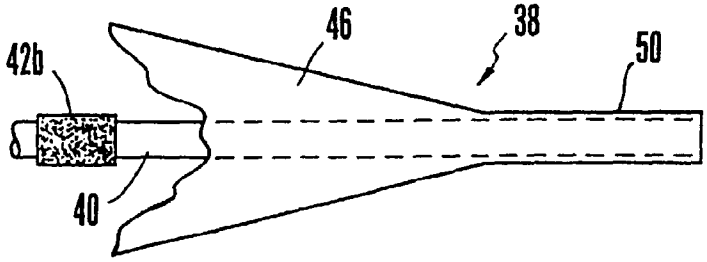


Fig. 3B

Fig. 4



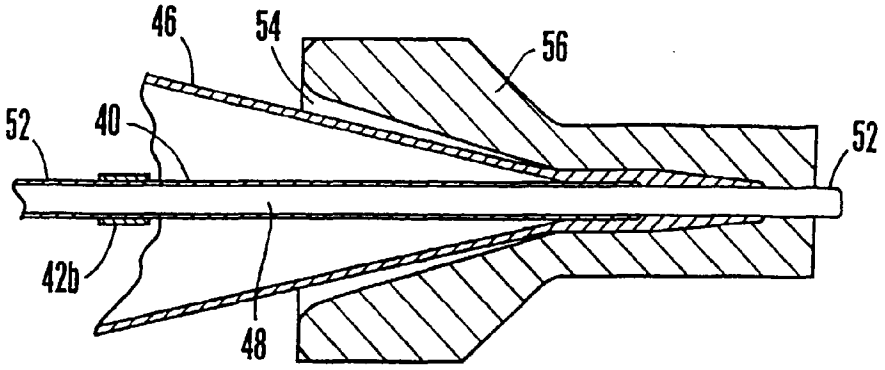


Fig. 5

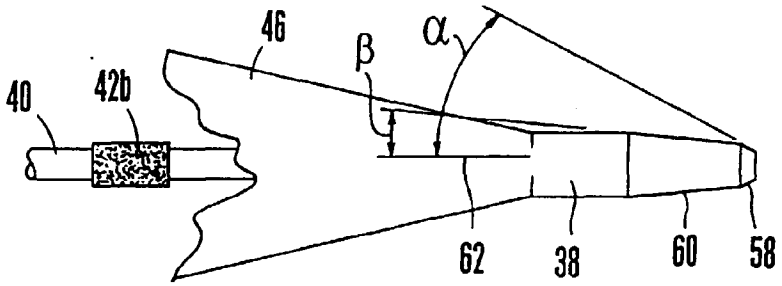


Fig. 6

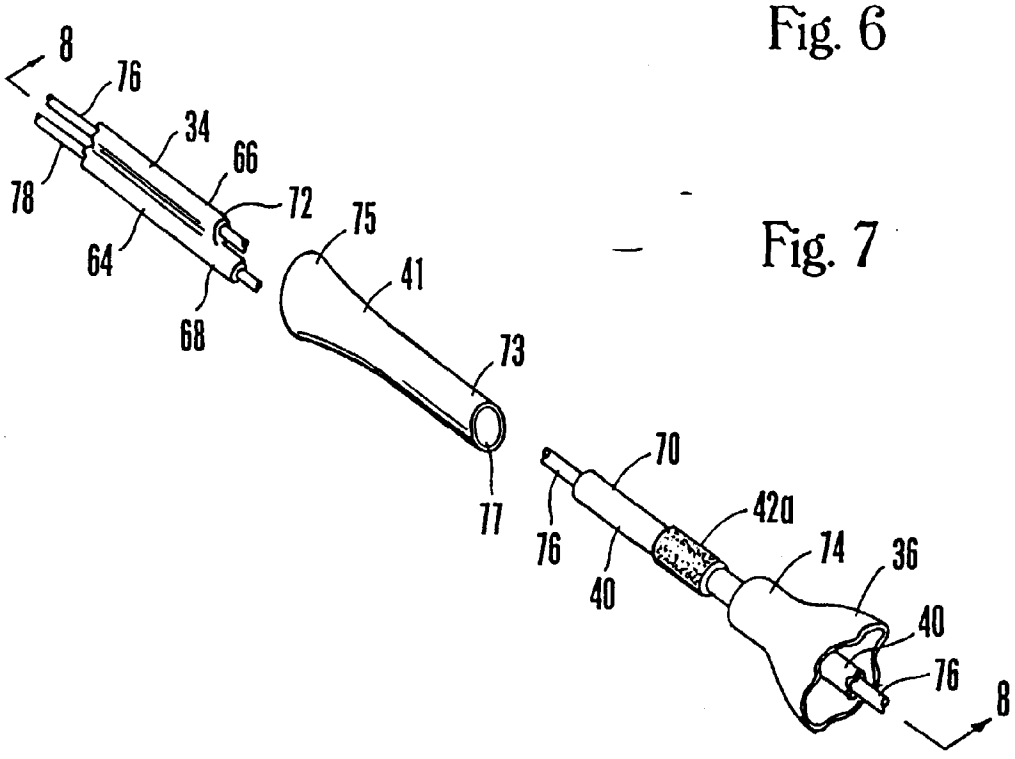


Fig. 7

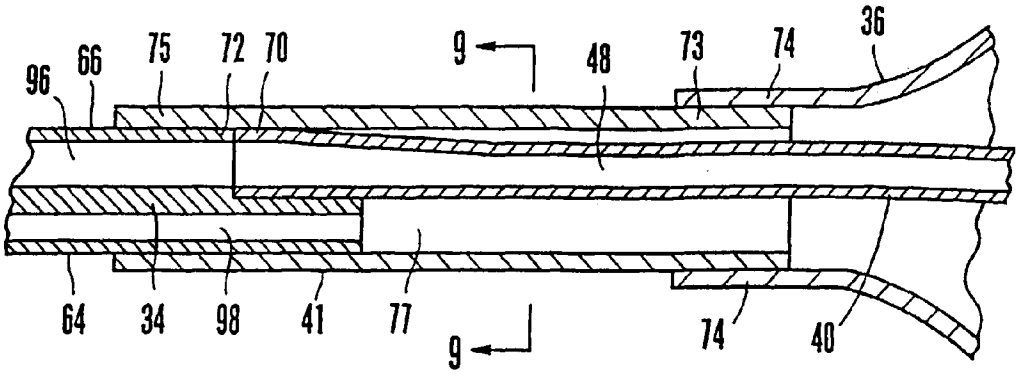


Fig. 8

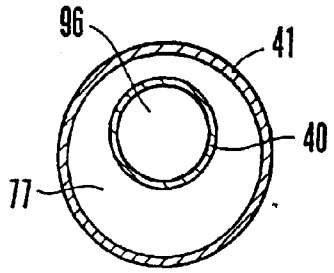


Fig. 9

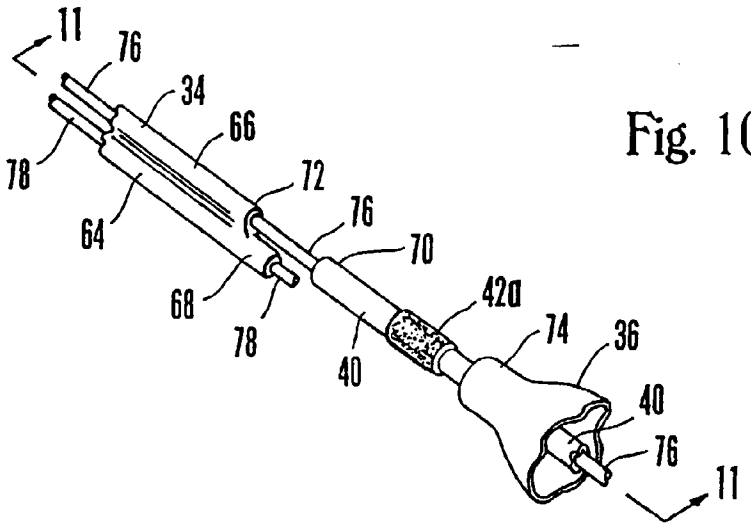


Fig. 10

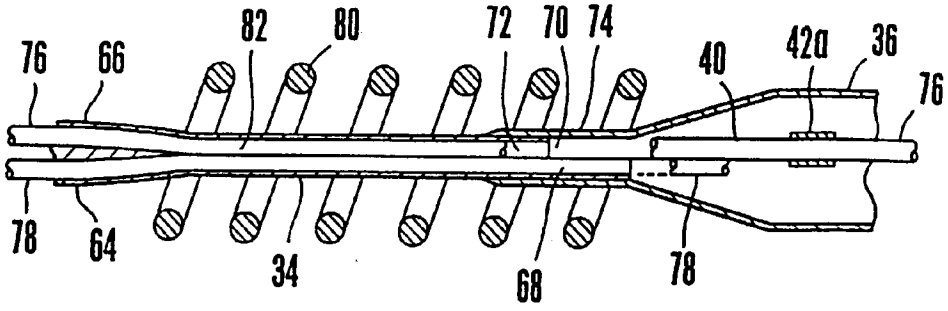

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Fig. 11

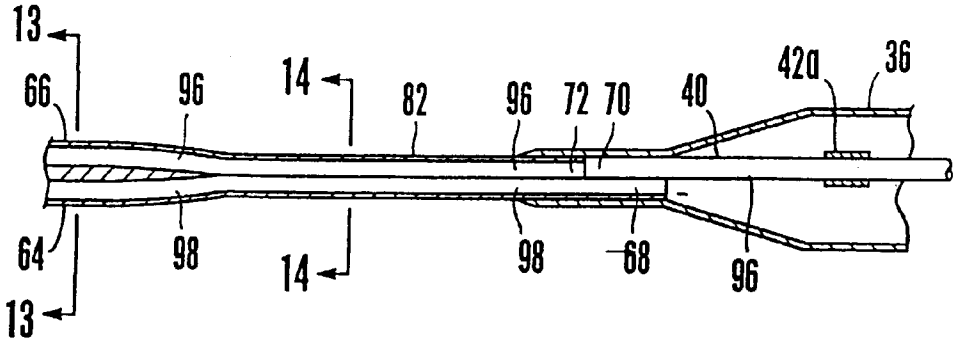
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Fig. 12

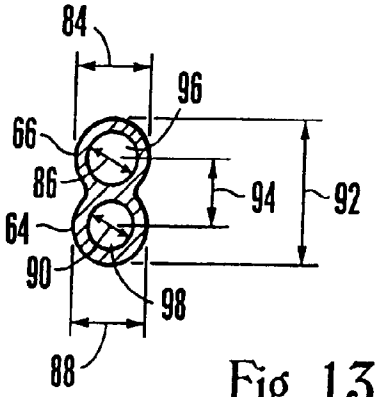

Fig. 13

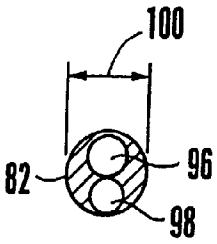

Fig. 14

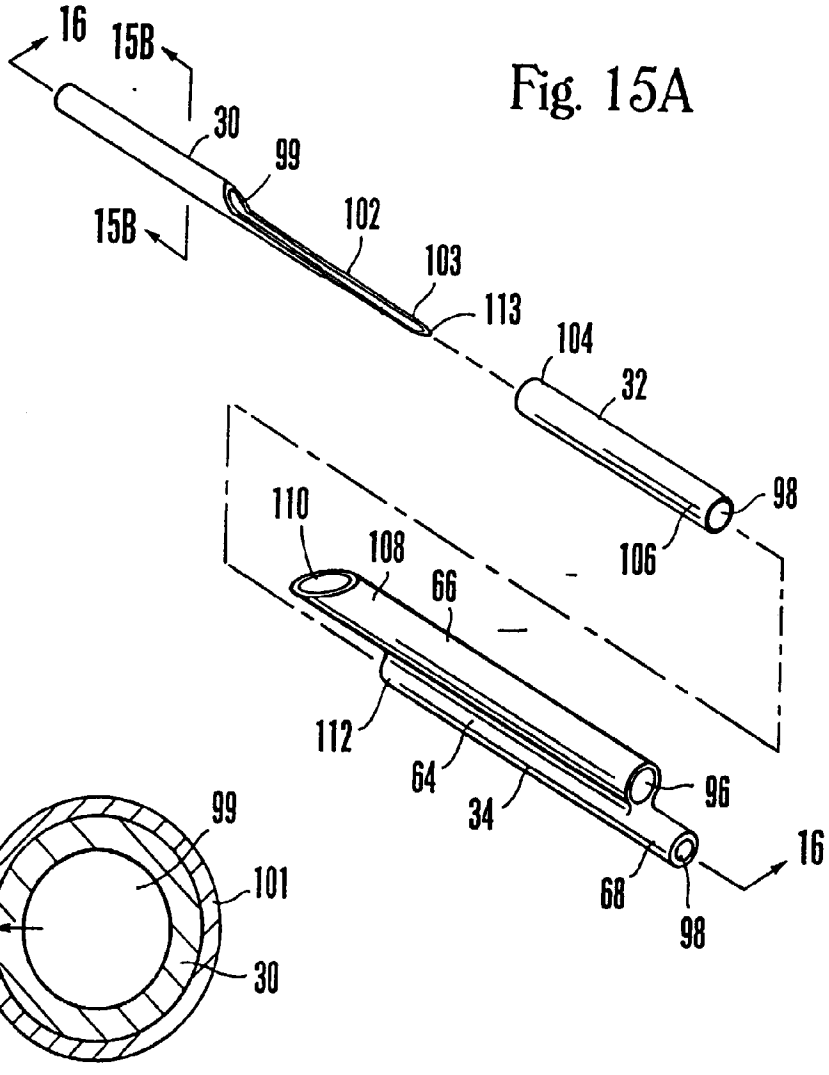

Fig. 15A

Fig. 15B

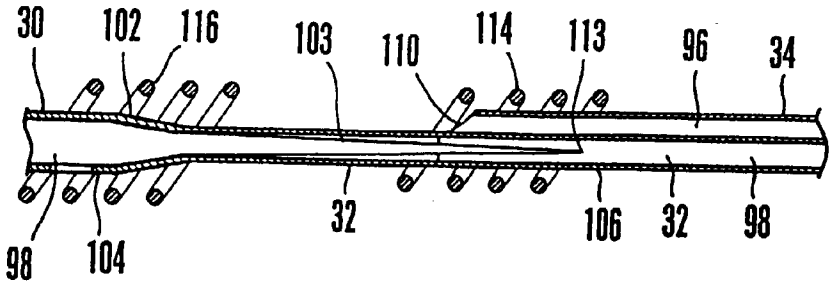

Fig. 16

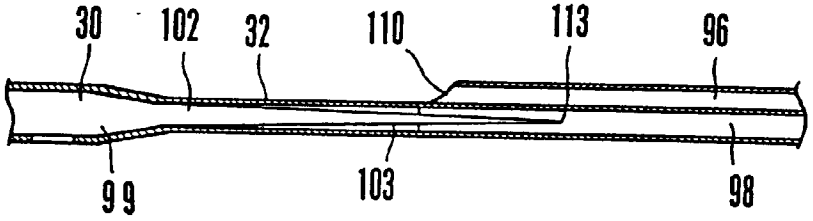

Fig. 17

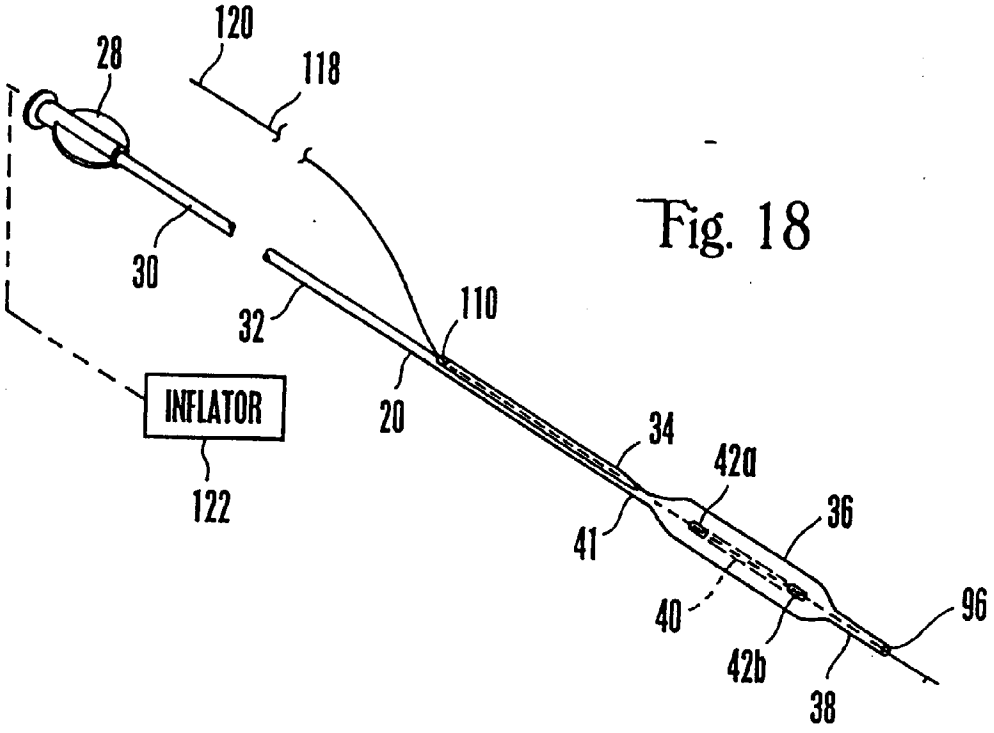

Fig. 18

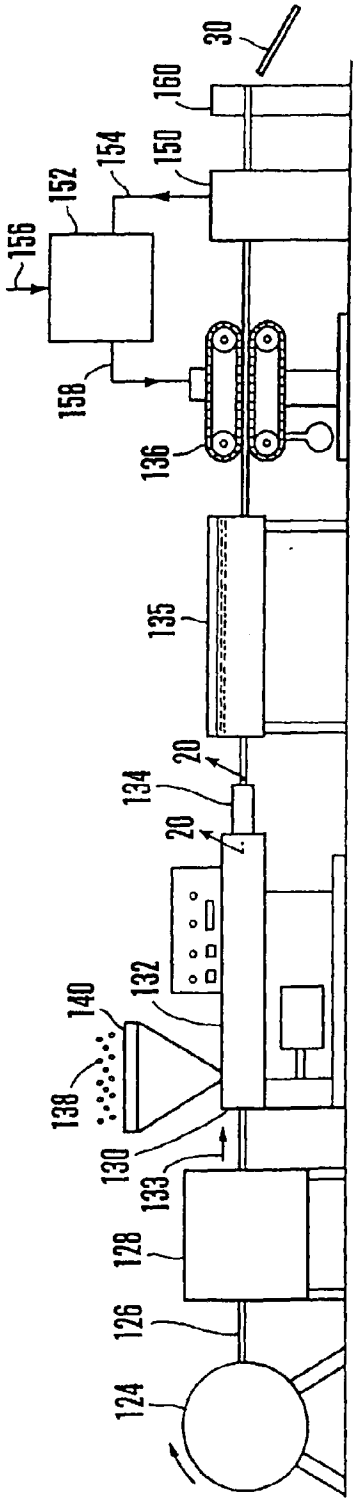
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Fig. 19

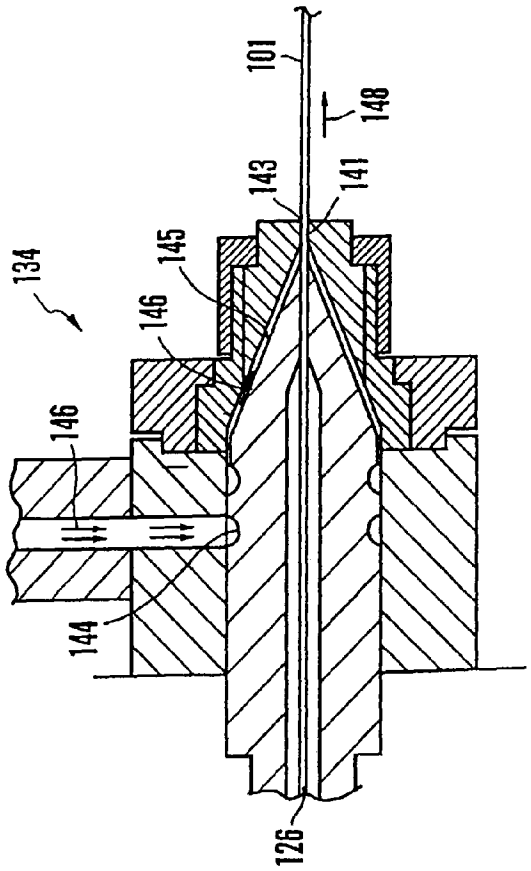
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Fig. 20

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Espacenet

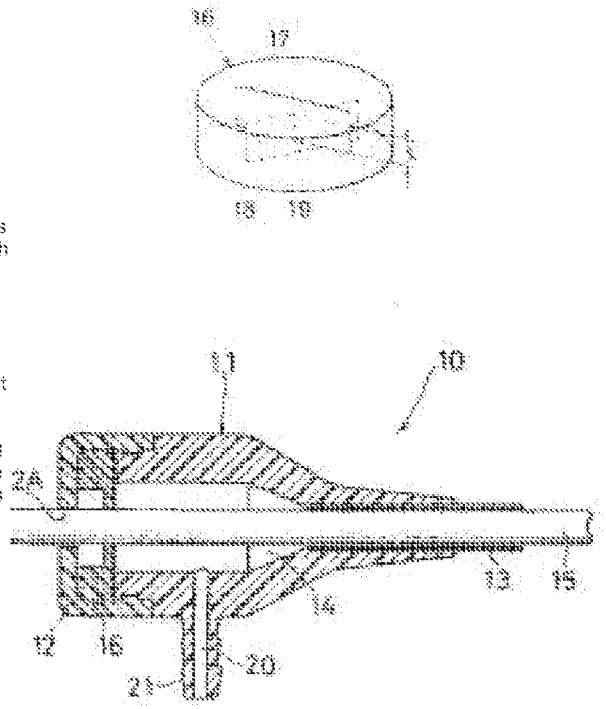
Bibliographic data: JP 59133877 (A)

VALVE ELEMENT

Publication date:	1984-08-01
Inventor(s):	MATSUMOTO ATSUSHI; SUZUKI TATSUO ÷
Applicant(s):	TERUMO CORP ÷
Classification:	**- international:** ***A61M25/08; A61M39/00; A61M39/06; A61M5/168; F16K15/14;*** (IPC1-7): A61M25/00; F16K15/14 **- European:** A61M39/06B
Application number:	JP19830005348 19830118
Priority number (s):	JP19830005348 19830118
Also published as:	• JP 2000949 (B) • JP 1573900 (C) • BE 898705 (A1)

Abstract of JP 59133877 (A)

PURPOSE:To provide a valve element with simple construction by carving a notch having its opening only at one of the end faces an another notch, only at the other end face in such a way that they intersect inside, by retaining rods with different diameters inserted in liquid-tight condition, and by forming proper shut condition immediately after a rod is drawn off. CONSTITUTION:A valve element 16 is made of soft resilient material such as silicon rubber, in which are carved No.1 notch 17 having its opening only at one of the end faces and No.2 notch 18, only at the other end face, where the two notches intersect inside the valve element 16.; While a cathetel 15 is inserted in a passage 14 of a lead-in tool 10 for medical use tubing, the valve element 16 is in facial contact closely with the perimeter of the cathetel 15, and thus the liquid-tight condition is maintained to ensure prevention of blood leakage from a flexible tube 13 inserted in a vessel. In order to remove the catheter 15 from said lead-in tool 10, the catheter 15 is drawn off from the valve element 16, and at the same time the notches 17, 18 shall form perfect shut condition so as to prevent outflow of blood.



Last updated: 12.10.2011 Worldwide Database 5.7.23.1; 92p

B31

Espacenet

Bibliographic data: JP 63255057 (A)

VALVE

Publication date:	1988-10-21
Inventor(s):	JIYAN KORON; PIEERU MARION +
Applicant(s):	JIYAN KORON; PIEERU MARION +
Classification:	**- international:** ***A61F2/24; F16K15/03;*** (IPC1-7): A61F2/24; F16K15/03
	- European: A61F2/24B
Application number:	JP19880067039 19880319
Priority number(s):	FR19870004107 19870320
Also published as:	• EP 0283413 (A1) • EP 0283413 (B1) • US 4908028 (A) • FR 2612597 (A1)

Abstract not available for JP 63255057 (A)
Abstract of corresponding document: EP 0283413 (A1)

The flap (3) is fixed angularly relative to at least one funicular elastic element (4) of which the ends extend towards the outside of this flap to pass at least partly through the ring (2) in order to pivot there, the free ends of the element (4) being anchored relative to the ring (2) in such a way as to constitute two torsion bars returning the flap (3) to its original position after it has been displaced.

Last updated: 12.10.2011 Worldwide Database 5.7.23.1; 92p

Espacenet

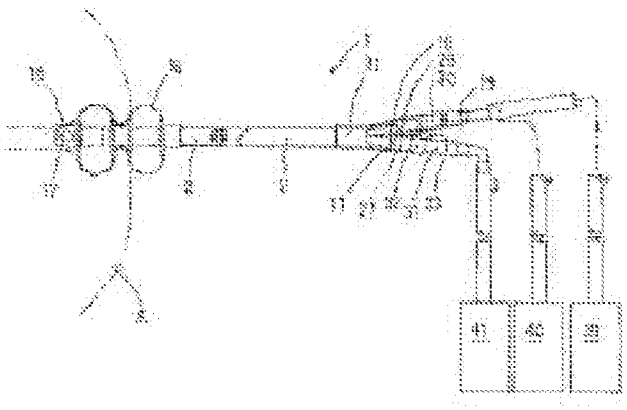
Bibliographic data: JP 9038197 (A)

RECTAL CATHETER

Publication date:	1997-02-10
Inventor(s):	TAKANE SHIGENOBU ÷
Applicant(s):	TAKANE SHIGENOBU ÷
Classification:	**- international:** ***A61M1/00; A61M25/00;*** (IPC1-7): A61M1/00; A61M25/00
	- European:
Application number:	JP19950209979 19950725
Priority number(s):	JP19950209979 19950725

Abstract of JP 9038197 (A)

PROBLEM TO BE SOLVED: To provide a rectal catheter which is capable of surely preventing the infection of a person receiving inspection with pathogenic bacteria, is extremely hygienic, improves the working efficiency of manufacturing work and contributes to a cost reduction. SOLUTION: The front end of a catheter body 2 integrally molded by delineating a contrast medium injecting path/air injecting path/excrement path and two air supplying paths therein is provided with two balloons. The air supplying paths communicate with these balloons 18. A corresponding connector for the contrast medium injecting path, a connector 10 for the air injecting path and a connector 11 for excretion are inserted into the opening ends of the respective passages at the base end of the catheter body 2. A contrast medium injecting tube 29, air injecting tube 30 and excrement injecting tube 31 corresponding to the respective connectors 10, 11 are connected thereto. A corresponding check valve for the contrast medium, check valve 26 for air and check valve 27 for excrement are mounted at the inside of the respective connectors 10, 11.



Last updated:
12.10.2011 Worldwide
Database 5.7.23.1, 92p

B33

Espacenet

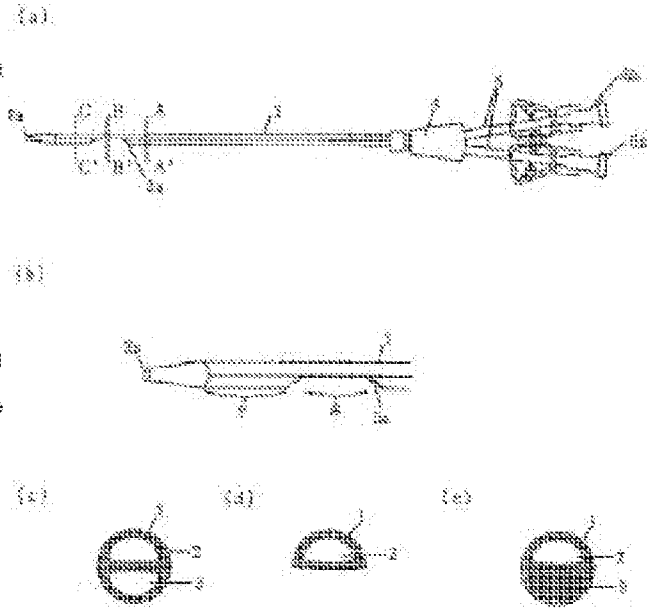
Bibliographic data: JP 2001340466 (A)

DOUBLE LUMEN CATHETER

Publication date:	2001-12-11
Inventor(s):	MIYAZAWA TOMOKO; KOIKE NORIO +
Applicant(s):	UNITIKA LTD +
Classification:	**- international:** ***A61M1/14; A61M25/00;*** (IPC1-7): A61M1/14; A61M25/00
	- European:
Application number:	JP20000160383 20000530
Priority number(s):	JP20000160383 20000530
Also published as:	• JP 4567847 (B2)

Abstract of JP 2001340466 (A)

PROBLEM TO BE SOLVED: To provide a double lumen catheter which has a shape of making aspiration defectiveness hard to occur in blood removal during extracorporeal circulation such as dialysis and enabling effective dialysis, and which can lighten both burden to an operator and a patient when the catheter is inserted. SOLUTION: The catheter body 1 of the double lumen catheter consists of a tube having a blood returning lumen 2 and a blood removal lumen 3 separated by a partition. A blood returning aperture 2a which is the aperture of the blood returning lumen 2 is provided at the tip of the catheter body 1, and a blood removal aperture 3a which is the aperture of the blood removal lumen 3 is provided at the location which is apart 3-11 cm from the tip of catheter body 1 to its base side.; The aperture face of the blood removal aperture 3a has an angle of 5-90 deg. to the long distance direction of the catheter body, and the configuration of the catheter body 1 from the position of the blood removal aperture to the tip side consists of a narrow diameter part 8 having a small cross section and a following wide diameter part 7 having a large cross section.



Last updated:
26.04.2011 Worldwide
Database 5.7.22; 93p

(19)日本国特許庁（ＪＰ）　(12) **公開特許公報**（Ａ）　(11)特許出願公開番号
特開2001－340466
（P2001－340466A）
(43)公開日　平成13年12月11日(2001.12.11)

(51)Int.Cl.[7]	識別記号	ＦＩ	テーマコード(参考)
Ａ６１Ｍ　25/00	４０５	Ａ６１Ｍ　25/00	４０５Ｂ　４Ｃ０７７
1/14	５３０	1/14	５３０

審査請求　未請求　請求項の数1　ＯＬ　（全　７　頁）

(21)出願番号　特願2000－160383(P2000－160383)

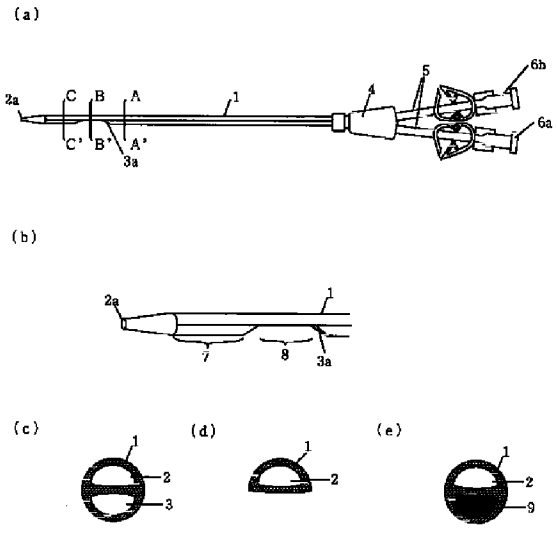
(22)出願日　平成12年５月30日(2000.5.30)

(71)出願人　000004503
ユニチカ株式会社
兵庫県尼崎市東本町１丁目50番地
(72)発明者　宮澤　智子
愛知県岡崎市日名北町４－１　ユニチカ株式会社岡崎工場内
(72)発明者　小池　紀夫
愛知県岡崎市日名北町４－１　ユニチカ株式会社岡崎工場内

Ｆターム(参考)　4C077 AA05 BB01 CC03 DD20 DD21 EE01 JJ03 KK25

(54)【発明の名称】　ダブルルーメンカテーテル

(57)【要約】
【課題】　透析等の体外循環時における脱血時に吸引不良が発生しにくく、透析等が効率的に行える形状を有し、しかも、カテーテルを挿入する際に術者及び患者の負担を軽くすることができるダブルルーメンカテーテルを提供する。
【解決手段】　隔壁により仕切られた返血ルーメン２と脱血ルーメン３を有するチューブをカテーテル本体１とするダブルルーメンカテーテルにおいて、返血ルーメン２の開口部である返血孔２ａをカテーテル本体１の先端部付近に設け、脱血ルーメン３の開口部である脱血孔３ａをカテーテル本体１の先端部から基部側に３～１１ｃｍ隔てた位置に設け、該脱血孔３ａの開口面がカテーテル本体の長手方向に対して５～９０°の角度を有しており、さらに脱血孔のある位置から先端側のカテーテル本体１の形状が、断面積の小さい狭径部８とそれに引続く断面積の大きい広径部７とからなっていることを特徴とするダブルルーメンカテーテル。



【特許請求の範囲】
【請求項1】　隔壁により仕切られた返血ルーメンと脱血ルーメンを有するチューブをカテーテル本体とするダブルルーメンカテーテルにおいて、返血ルーメンの開口部である返血孔をカテーテル本体の先端部付近に設け、脱血ルーメンの開口部である脱血孔をカテーテル本体の先端部から基部側に3～11cm隔てた位置に設け、該脱血孔の開口面がカテーテル本体の長手方向に対して5～90°の角度を有しており、さらに脱血孔のある位置から先端側のカテーテル本体の形状が、断面積の小さい狭径部とそれに引続く断面積の大きい広径部とからなることを特徴とするダブルルーメンカテーテル。
【発明の詳細な説明】
【0001】
【発明の属する技術分野】本発明は、透析療法などに使用されるダブルルーメンカテーテルに係り、さらに詳しくは、カテーテルを留置する際、術者および患者に負担が少なく透析等を良好に行うのに適した形状を有するダブルルーメンカテーテルに関するものである。
【0002】
【従来の技術】緊急透析、薬物中毒、劇症肝炎等の短期間の血液浄化療法で必要とされる血液透析などの体外循環治療（ブラッドアクセス）の手段として、一方のルーメンで血液を体外に排出し、もう一方のルーメンで浄化した血液を体内に戻すダブルルーメン型カテーテルが汎用されている。この方法はシャントへの移行前で、カテーテル留置直後から透析療法が行え、カテーテルの挿入及び留置箇所が一箇所で済む（動・静脈ルートが1本でとれる）ため患者への負担が少ないという利点もある。
【0003】従来使用されている大半のブラッドアクセス用ダブルルーメンカテーテルにおける脱血ルーメン側の脱血孔の形状は、図6に示したようなカテーテル側面に穴（側孔）を開けたものであった。
【0004】
【発明が解決しようとする課題】近年、患者の高齢化や糖尿病性腎症の増加に伴い透析患者の血管が脆く、狭くなる傾向にあり、カテーテル側面に穴（側孔）を開けた従来の形状では、透析中の吸引圧によりカテーテルの脱血ルーメンが血管壁にへばり付き、血液を体外に排出できない脱血不良を招く場合が増大するという問題があった。
【0005】この問題を解決するため、図7に示したような脱血孔がカテーテルの長手方向に対し垂直に開いているエンドホールタイプのものが提案され、実際に製品化されているものもある。
【0006】一般的にカテーテルを留置する方法として、出血量を最小限に抑え、できる限り迅速に留置する必要があることから、予め血管の所定の位置まで挿入されたガイドワイヤーに沿ってカテーテルを挿入、留置する方法（セルジンガー法）が採られることが多い。
【0007】脱血孔がエンドホールタイプのダブルルーメンカテーテルはカテーテルの先端に段差を有するので、セルジンガー法による留置では脱血孔部分の段差が穿刺部に引っかかり血管内に挿入できない。このためエンドホールタイプのカテーテルを留置する際は、まずカテーテルよりも太いシースを穿刺しその内腔にカテーテルを挿入する方法が採られるが、この方法ではカテーテルを留置する血管が太い血管に限定され、また刺入部が大きくなるため留置時の出血が多く止血も難しくなり感染の機会も増えるという問題があった。
【0008】一方、図7に示すカテーテルの問題点を解決するため、図8に示したような脱血孔がカテーテルの長手方向に対し斜めに開いているものも提案され製品化されている。このカテーテルの形状によればセルジンガー法によるカテーテルの留置操作が可能となるが、依然としてカテーテル先端に段差あるためカテーテルを血管に挿入する際血管の内壁を傷つける可能性があった。
【0009】本発明は、上記のような課題を解決し、カテーテルを留置する際、術者および患者に負担が少なく、透析等を良好に行うのに適した形状を有するダブルルーメンカテーテルを提供することを目的とするものである。
【0010】
【課題を解決するための手段】本発明者らは、上記課題を解決するため鋭意検討の結果、カテーテル先端部から基部側へずれた位置に、カテーテルの長手方向に対し斜めに脱血孔を設け、その脱血孔より先端側のカテーテル本体の形状を特殊な形状に工夫することにより、血管壁の脱血孔へのへばり付きを防ぎ、かつ血管内への挿入がスムーズできることを見出し、本発明に到達した。
【0011】すなわち、本発明は、隔壁により仕切られた返血ルーメンと脱血ルーメンを有するチューブをカテーテル本体とするダブルルーメンカテーテルにおいて、返血ルーメンの開口部である返血孔をカテーテル本体の先端部付近に設け、脱血ルーメンの開口部である脱血孔をカテーテル本体の先端部から基部側に3～11cm隔てた位置に設け、該脱血孔の開口面がカテーテル本体の長手方向に対して5～90°の角度を有しており、さらに脱血孔のある位置から先端側のカテーテル本体の形状が、断面積の小さい狭径部とそれに引続く断面積の大きい広径部とからなることを特徴とするダブルルーメンカテーテルを要旨とするものである。
【0012】
【発明の実施の形態】以下、本発明を詳細に説明する。本発明のダブルルーメンカテーテルは、構成部材として、返血ルーメンと脱血ルーメンが形成されているカテーテル本体、分岐部及び体外循環回路や輸液回路等へ接続するための枝管（または延長管）からなり、枝管の先端にはコネクターが付いている。返血ルーメンは体外循環の返血用ルーメンであり、脱血ルーメンは体外循環の

脱血用ルーメンである。本発明のダブルルーメンカテーテルは、カテーテル本体の先端側の形状に特徴を有するものであり、分岐部、枝管及びコネクターについては従来から知られているものが良好に用いられる。

【００１３】また、カテーテル本体の材質としては、ポリウレタン、ポリ塩化ビニル、シリコーン、ポリエチレン、ポリプロピレン、エチレン－酢酸ビニル共重合体、ポリアミド等で血管内で安定な形状を保ち血管を傷つけない硬さのものであれば何でも良いが、特にポリウレタンはカテーテル挿入性を損なわない程度の硬さを持ち、常温では硬く体内の温度では柔らかくなる性質を持つので最も好ましい。

【００１４】カテーテルの枝管の材質としては、カテーテル本体の材質と同じ硬さの材質あるいは柔らかい材質が使用される。例えばポリウレタン、ポリ塩化ビニル、シリコーン、エチレン－酢酸ビニル共重合体等が挙げられるが、容易に折れ曲がり内腔が閉塞しない強度と皮膚表面を傷つけない柔らかさを持つ樹脂としてポリウレタン、ポリ塩化ビニル、シリコーンが特に好ましい。

【００１５】コネクターの材質としては、硬度、強度が高く、消毒剤等に対する耐薬品性と寸法安定性に優れた樹脂で、成形され得るものであれば良い。この樹脂としては、例えばポリカーボネート、硬質のポリ塩化ビニル、ポリウレタン、ポリアミド、ポリエーテルイミド、またはこれらの樹脂に強度をさらに上げるためにほかの樹脂を混合させたものであっても良い。

【００１６】次に、本発明のダブルルーメンカテーテルを図面を用いて説明する。図１（ａ）は、本発明のダブルルーメンカテーテルの一例を示したものである。カテーテル本体１の基部側に分岐部４を介して枝管５が延び、枝管５の先にコネクター６が付いている。図１（ｂ）はカテーテル本体１の先端側の拡大図である。カテーテル本体１の先端部付近には、基部から先端部まで貫通する返血ルーメン２の返血孔２ａが設けられ、先端から基部側へ一定の距離だけ離れた箇所に脱血ルーメン３に通じる脱血孔３ａが設けられている。脱血ルーメンは、脱血孔３ａからカテーテル本体基部まで貫通している。脱血孔３ａがある位置からカテーテル本体の先端側に断面積の小さい狭径部８と、それに引続き断面積の大きい広径部７とが形成されている。

【００１７】本発明において、脱血孔３ａの位置は、カテーテル本体の先端から基部側に３～１１ｃｍ隔てられた箇所である必要がある。３ｃｍより短いと、返血孔２ａから体内に戻される浄化された血液を再び透析回路に送ることになり、逆に１１ｃｍより長くなると、カテーテルの有効長が長くなり、留置する血管が限られるため、採用できない。また、好ましくは３～８ｃｍであり、より好ましくは３．５～５ｃｍである。

【００１８】本発明における脱血孔３ａは、その開口面がカテーテル本体１の長手方向と５～９０°の角度を有するように設けられていることが必要である。５°より小さいと透析中の吸引圧により血管壁が脱血孔３ａにへばりついて塞がれるおそれがあり採用できない。また９０°より大きいとカテーテルを体内に挿入する際に脱血孔３ａが血管を傷つけるおそれがあるので採用できない。この角度は、好ましくは１５～６０°であり、より好ましくは３０～４５°である。

【００１９】本発明においては、脱血孔３ａがある位置より先端側のカテーテル本体が、断面積の小さい狭径部８と、それに引続く断面積の大きい広径部７とになっていることが必要である。図１（ｃ）（ｄ）（ｅ）は、それぞれ、図１（ａ）で示したＡ－Ａ’断面、Ｂ－Ｂ’断面、Ｃ－Ｃ’断面を示しており、図中に半円形状の返血ルーメン２と脱血ルーメン３が示されている。狭径部８は、脱血孔３ａがある位置のカテーテル本体の断面積より小さければよく、特に形状は限定されないが、例えば図１（ｄ）に示されているように返血ルーメンのみからなる半円形状が挙げられる。狭径部８の長さとしては、０．２～１０ｃｍが望ましく、１～３ｃｍがより望ましい。０．２ｃｍより短いと、脱血孔３ａが血管壁にへばりつき易くなるため、脱血不良を招き、１０ｃｍより長くなると有効長が長くなり、留置する血管が限られる。

【００２０】また、広径部７は、上記した狭径部８より断面積が大きければよく特にその形状は限定されないが、好ましくは円形であり、例えば図１（ｅ）に示されているように、返血ルーメン２に併設してカテーテル本体１と同じ材質の詰め物９により半円形状に成形すればよい。または脱血ルーメンを溶封することにより広径部７を成形することもできる。広径部７の長さとしては、０．２～１０ｃｍが望ましく、１～３ｃｍがより望ましい。０．２ｃｍより短いと、強度が弱くなり、１０ｃｍより長くなると有効長が長くなるため留置する血管が限られる。

【００２１】狭径部８と、それより先端側の広径部７との境目は、カテーテル本体１の長手方向に対して脱血ルーメン３の脱血孔３ａと同様に５～９０°の角度を有するようにするのが好ましく、特に３０～４５°の角度を有することが好ましい。

【００２２】図１（ｂ）では、カテーテル本体の先端部が円錐状になっているが、カテーテルの血管への挿入性に優れるためであり、本発明では先端部の形状を適宜変形したものも含まれる。

【００２３】図２（ａ）（ｂ）は、本発明の他の例を示したのもであり、カテーテル本体１の広径部７の側面に返血ルーメンに通じる３個の返血孔側孔２ｂを設けたものである。

【００２４】また、図３（ａ）（ｂ）は、本発明の他の例を示したものであるが、脱血ルーメン３の脱血孔３ａより基端側には万一脱血孔3aが閉塞した場合に備え脱血孔側孔３ｂを１個設けたものである。この側孔３ｂの

直径は脱血ルーメン３の直径より小さく、形状は楕円形または円形がよい。

【００２５】

【実施例】次に、実施例によって具体的に説明する。なお、実施例中の評価方法は次のとおりである。

（カテーテル側孔の血管壁へばり付き試験）図５のように塩化ビニル製で内径６ｍｍのチューブ１０の途中に厚さ０．０２ｍｍのポリエチレン製のフィルムからなる筒１１をはさんだ管を血管に見立て、ポリエチレン製のフィルムからなる筒１１部より上流側の塩化ビニル製のチューブ１０の部分に、脱血孔３ａまたは側孔３ｂがポリエチレン製のフィルムからなる筒１１部に位置するようにカテーテル1を差し込んだ。血管に見立てたチューブ内には１分間に２５０ｍＬ流れる速さで３７℃の水１２をポンプ（日機装株式会社製型式ＢＰ－21Ｂ）１３にて送り、脱血及び返血側アダプター６には透析回路用チューブ（泉工医科工業株式会社製）１４を接続させ、脱血側アダプター６ａと透析用ポンプ（日機装株式会社製型式DCS－26）１５までの間にカテーテルが水を吸引する圧力（吸引圧）をモニターできるよう圧力計（株式会社岡野製作所製型式ＧＰM104N14）１６を取り付け、透析ポンプで吸引して脱血孔３ａがポリエチレン製のフィルムからなる筒１１にへばりつく時の吸引圧を測定した。

【００２６】実施例１

図１のようにポリウレタン製のカテーテル本体１(外径3.7㎜、長さ150㎜)と体外部の2本の枝管５（外径4㎜、長さ50㎜）とからなるダブルルーメンカテーテルで、脱血ルーメン3の脱血孔3ａがカテーテル本体１の長手方向に対して３０°の角度を有し、断面が返血ルーメン2のみの半円形状の狭径部８を１５ｍｍとし、狭径部８と広径部７との境目は、カテーテル本体１の長手方向に対して３０°の角度を有するダブルルーメンカテーテルを作製した。

【００２７】実施例２

図４のようにポリウレタン製のカテーテル本体１(外径3.7㎜、長さ150㎜)と体外部の２本の枝管５（外径4㎜、長さ50㎜）とからなるダブルルーメンカテーテルで、脱血ルーメン3の脱血孔3ａがカテーテル本体１の長手方向に対して３０°の角度を有し、断面が返血ルーメン2のみの半円形状の狭径部８を１５ｍｍとし、狭径部８と広径部７との境目は、カテーテル本体１の長手方向に対して３０°の角度を有し、返血孔２ａから基部側へ向かって９ｍｍ及び１５ｍｍの位置に長径３ｍｍ短径１．２ｍｍの楕円径の側孔２ｂを３個設け、脱血孔３ａより３ｍｍ基部側へ直径１ｍｍの円形の側孔３ｂを１個有するダブルルーメンカテーテルを作製した。

【００２８】比較例1

図６のようにポリウレタン製のカテーテル本体１(外径3.7㎜、長さ150㎜)と体外部の２本の枝管５（外径4㎜、長さ50㎜）とからなるダブルルーメンカテーテルで、返血孔２ａから基部側へ向かって９ｍｍ及び１５ｍｍの位置に長径３ｍｍ短径１．２ｍｍの楕円径の側孔２ｂを、返血孔２ａから基部側へ向かって３４ｍｍ、４１ｍｍ及び４８ｍｍの位置の脱血ルーメン側には長径３ｍｍ短径１．２ｍｍの楕円径の側孔３ｂを有するダブルルーメンカテーテルを作製した。

【００２９】実施例１、実施例２及び比較例のダブルルーメンカテーテルについてカテーテル側孔の血管壁へばり付き試験を行ったが、それぞれ流量２５０ｍＬ／ｍｉｎの時のカテーテルにへばりついたときの吸引圧を測定したところ、比較例１のカテーテルは2×10^4Ｐａの吸引圧でカテーテルがへばりついたが、実施例１及び２のカテーテルは2×10^4Ｐａ以上の吸引圧を上げてもカテーテルがフィルムにへばりつくことはなかった。

【００３０】

【発明の効果】本発明によれば、患者の血液を体外へ排出する際に生じる吸引圧が高い場合においても、カテーテルの脱血孔での患者の血管壁へのへばり付きを防止することにより、脱血不良が改善され、またカテーテルを挿入する際に術者及び患者の負担を軽くすることができる。さらに、脱血孔から先端側のカテーテル本体の断面形状を一旦半円形状にして再び円形状にすることで、カテーテル本体の血管壁へのへばり付き防止効果が更に高まる。

【図面の簡単な説明】

【図１】本発明のダブルルーメンカテーテルの一例を示す模式図、要部の拡大図及びＡ－Ａ’、Ｂ－Ｂ’、Ｃ－Ｃ’の断面図である。

【図２】本発明のダブルルーメンカテーテルの他の例を示す模式図及び要部の拡大図である。

【図３】本発明のダブルルーメンカテーテルの他の例を示す模式図及び要部の拡大図である。

【図４】本発明のダブルルーメンカテーテルの他の例を示す模式図及び要部の拡大図である。

【図５】本発明におけるカテーテル側孔の血管壁へばり付き試験のモデルを示す概略図である。

【図６】従来のダブルルーメンカテーテルの一例を示す模式図及び要部の拡大図である。

【図７】従来のダブルルーメンカテーテルの他の例を示す模式図及び要部の拡大図である。

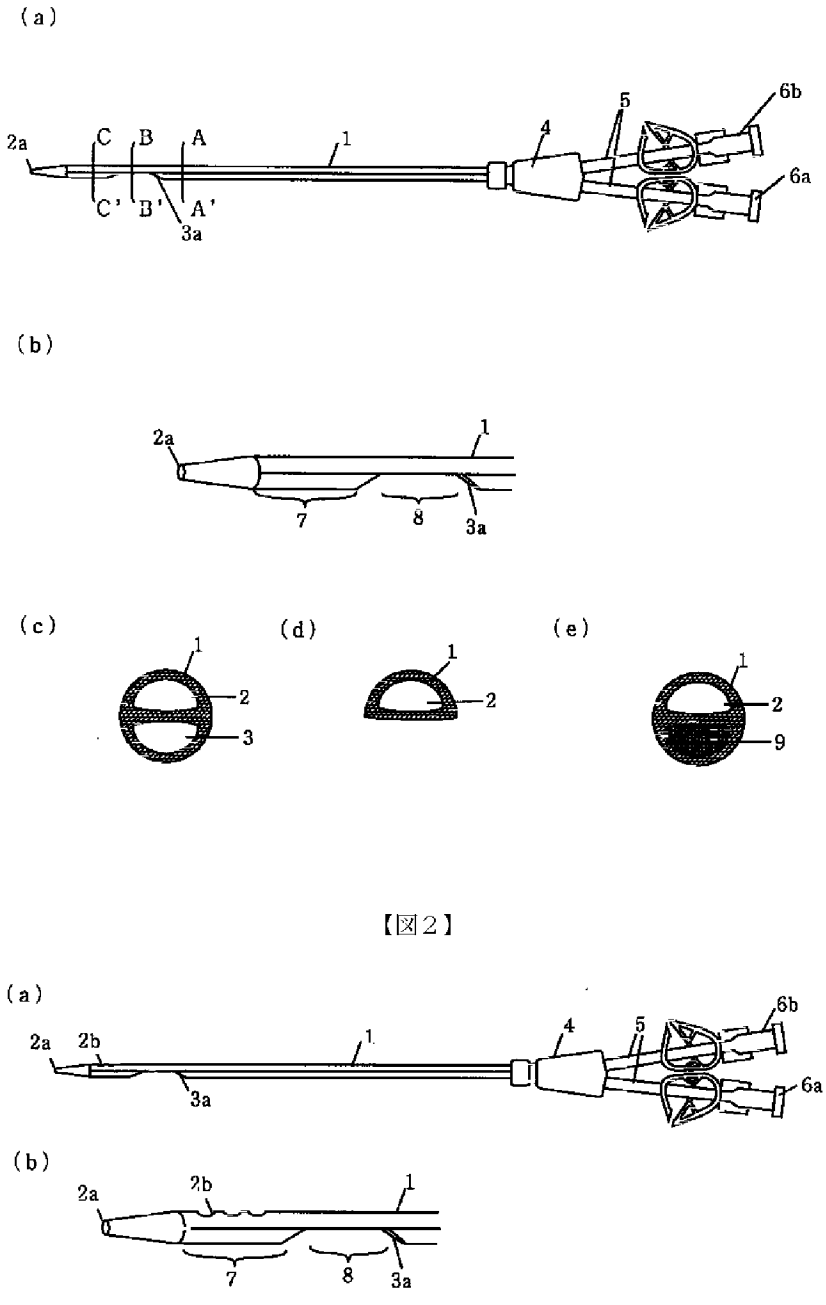
【図８】従来のダブルルーメンカテーテルの他の例を示す模式図及び要部の拡大図である。

【符号の説明】

１　カテーテル本体
２　返血ルーメン
２ａ　返血孔
２ｂ　返血孔側孔
３　脱血ルーメン
３ａ　脱血孔

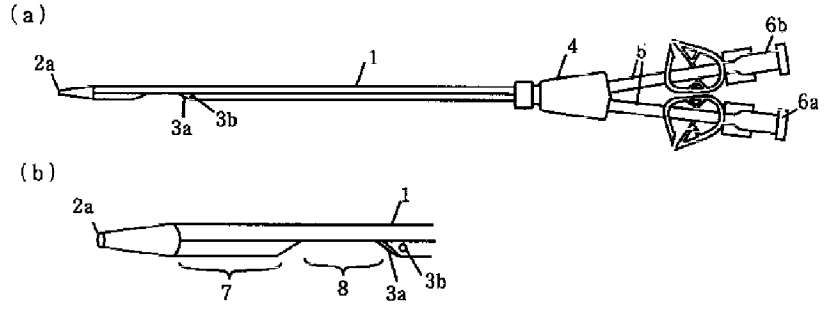
３ｂ　脱血孔側孔
４　カテーテルと枝管の分岐部
５　枝管
６ａ　脱血側コネクター
６ｂ　返血側コネクター
７　広径部
８　狭径部
９　詰め物
１０　塩化ビニル製のチューブ
１１　ポリエチレン製のフィルムからなる筒
１２　水
１３　ポンプ
１４　透析回路用チューブ
１５　透析用ポンプ
１６　圧力計

【図１】

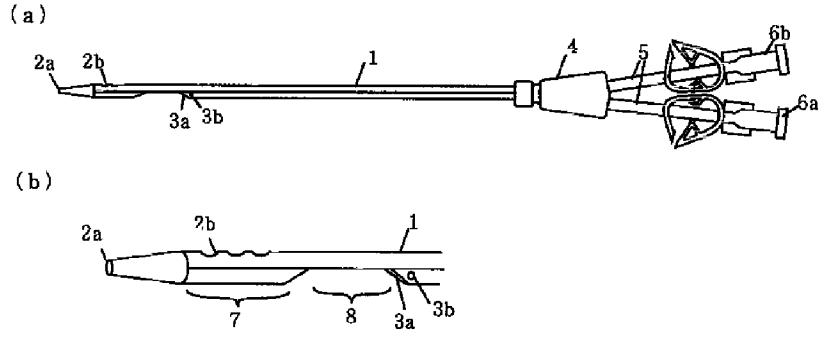


【図２】

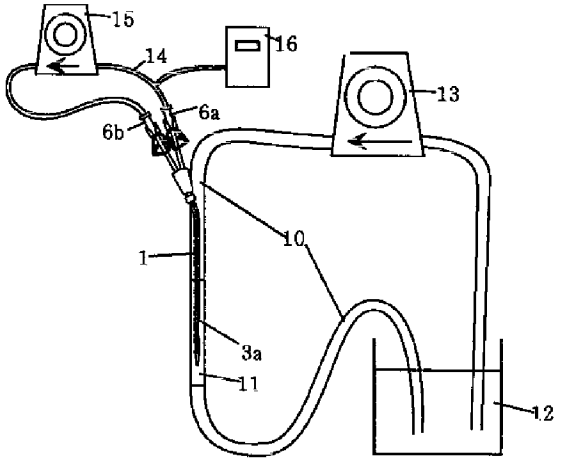
【図3】


(a)
2a
1
4
5
6b
6a
3a
3b
(b)
2a
1
7
8
3a
3b

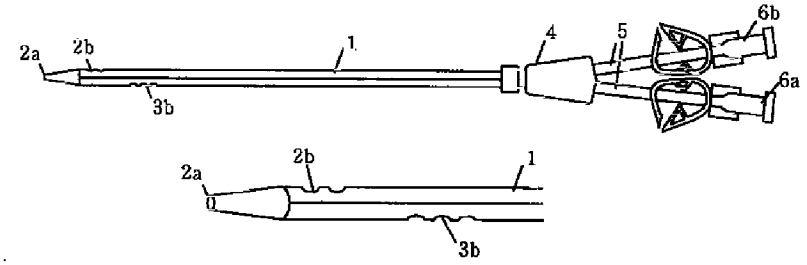
【図4】


(a)
2a
2b
1
4
5
6b
6a
3a
3b
(b)
2a
2b
1
7
8
3a
3b

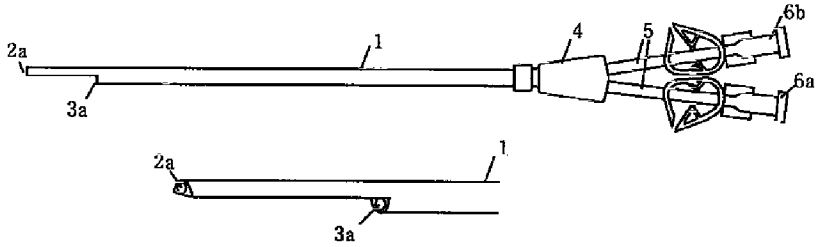
【図5】


15
14
16
13
6a
6b
10
1
3a
11
12

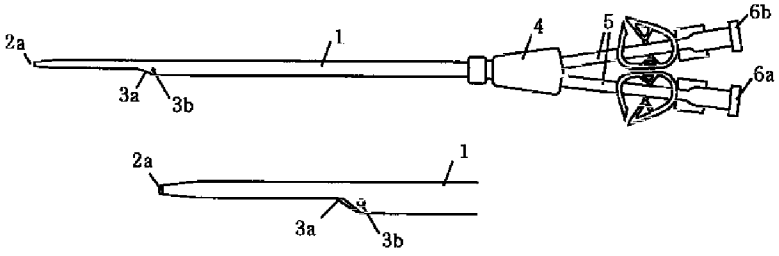
【図6】


2a
2b
1
4
5
6b
6a
3b
2a
2b
1
3b

【図7】


2a
1
4
5
6b
6a
3a
2a
1
3a

【図8】


2a
1
4
5
6b
6a
3a
3b
2a
1
3a
3b

B34

Espacenet

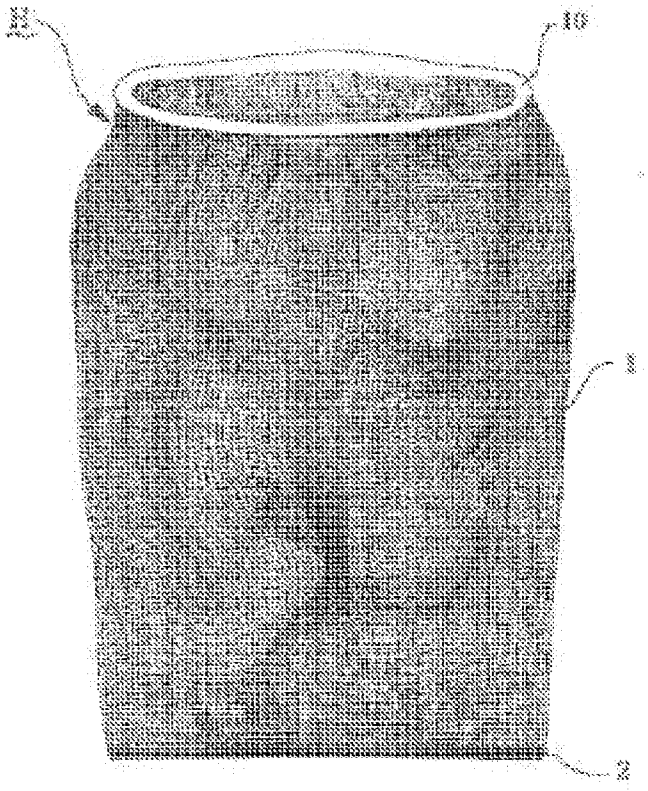
Bibliographic data: JP 2001172848 (A)

BIODEGRADABLE AND SIMPLE CIRCULAR KNIT BAG

Publication date:	2001-06-26
Inventor(s):	MIYAMOTO TAKETOSHI +
Applicant(s):	MIYAGEN KK +
Classification:	**- international:** ***B65D30/04; B65D65/46; B65F1/00; D04B1/16; D04B1/22;*** (IPC1-7): B65D30/04; B65D65/46; B65F1/00; D04B1/16 **- European:**
Application number:	JP19990353566 19991213
Priority number (s):	JP19990353566 19991213
Also published as:	• JP 4400972 (B2)

Abstract of JP 2001172848 (A)

PROBLEM TO BE SOLVED: To provide a simple circular knit bag not having a sewn part at all, being inexpensive and durable, and having biodegradability. SOLUTION: The following means are employed: the bottom part 2 of the circular knit bag is previously knitted in the edge part of a bag body part 1; a fusing thread with the lower melting point than a thread composing the body part 1 is fused by heating in order to perform the fusing between the composing threads to form the bag, and the threads composing the body part 1 and the fusing thread comprise a biodegradable polymer. Thus, the bag is easily biodegraded by microorganisms, and wet refuse such as garbage can be buried in the ground or thrown into a composting apparatus together with the bag.



Last updated: 26.04.2011 Worldwide Database 5.7.22; 93p

(19)日本国特許庁（ＪＰ）　(12) 公開特許公報（Ａ）　(11)特許出願公開番号
特開2001－172848
(P2001－172848A)
(43)公開日　平成13年６月26日(2001.6.26)

(51)Int.Cl.[7]	識別記号	ＦＩ		テーマコード(参考)
Ｄ０４Ｂ　1/16		Ｄ０４Ｂ　1/16		３Ｅ０２３
Ｂ６５Ｄ　30/04		Ｂ６５Ｄ　30/04		３Ｅ０６４
65/46		65/46		３Ｅ０８６
Ｂ６５Ｆ　1/00		Ｂ６５Ｆ　1/00	Ｊ	４Ｌ００２
	１０２		１０２Ｚ	

審査請求　未請求　請求項の数３　ＯＬ　（全　６　頁）　最終頁に続く

(21)出願番号　特願平11－353566

(22)出願日　平成11年12月13日(1999.12.13)

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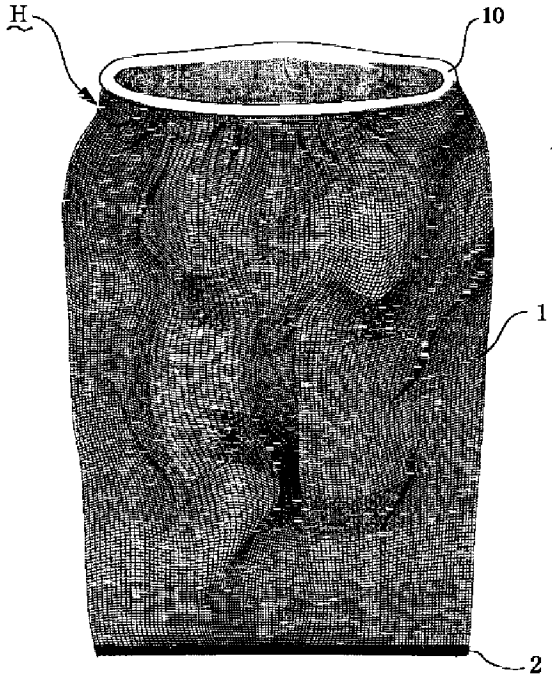
(54)【発明の名称】　生分解性簡易丸編み袋

(57)【要約】
【課題】　縫製箇所が全く無く安価で丈夫な生分解性を有する簡易丸編み袋を提供すること。
【解決手段】　丸編み袋の袋底部２が、袋胴部１端部に予め編み込まれてある、当該袋胴部１を構成している糸よりも低融点の溶着糸を加熱溶着せしめて当該構成糸同士を溶着接合して形成されており、かつ、これら袋胴部１の構成糸および溶着糸が生分解性高分子を含んでいるという手段を採用した。
【効果】　微生物によって簡単に分解されるので、厨芥等の生ゴミを袋ごと土中に埋めたり、堆肥化装置に入れることができる。



【特許請求の範囲】
【請求項１】　筒状の丸編生地から成る袋胴部１と、この袋胴部１の端部の生地同士を接合した袋底部２とから成る丸編み袋であって、
この袋底部２が、袋胴部１の端部に予め編み込まれてある、当該袋胴部１を構成する糸よりも低融点の溶着糸Ｍを加熱溶着せしめることにより袋胴部１の端部を溶着接合して形成されており、かつ、これら袋胴部１の構成糸および溶着糸Ｍが生分解性高分子を含むことを特徴とした生分解性簡易丸編み袋。
【請求項２】　袋胴部１の構成糸および溶着糸Ｍが、生分解性脂肪族ポリエステル糸であることを特徴とした請求項１記載の生分解性簡易丸編み袋。
【請求項３】　袋胴部１の端部の生地が局部的に収束した状態で溶着糸Ｍにより溶着接合されて袋底部２が形成されていることを特徴とした請求項１または請求項２記載の生分解性簡易丸編み袋。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、生分解性簡易丸編み袋、より詳しくは、縫製箇所が全く無く安価で丈夫な生分解性を有する簡易丸編み袋に関するものである。
【０００２】
【従来の技術】最近、調理場、台所等の流し台用の水切りゴミ袋として、編地にて製袋された簡易編袋が多用されている。この簡易編袋は、従来の多数の細孔を明けた合成樹脂フィルム製のゴミ袋に比べて格段に水切り性に優れており、また、伸縮自在であるところから、流し台の排水口やバスケット（通称三角コーナー）にも簡単に装着することができ、更には、再生繊維から製袋できるので、資源の有効利用を図るにも都合が良い。
【０００３】しかしながら、従来の編地袋は、製袋時に袋の底辺または側辺を接合するための手間の掛かる縫製処理を施さねばならず、この縫製作業が編地袋の製造コストを押し上げる結果となっていた。
【０００４】更にまた、従来の編地袋は、ポリエチレン等のポリオレフィン系樹脂繊維等で構成されていたため、使用後に焼却処理する場合には、炭酸ガスの発生量が多いことや高温燃焼による焼却炉の損傷の問題が避けられず、土中に埋立廃棄する場合にも、微生物等によって分解されずに半永久的に残存し、例えば、袋内の生ゴミの堆肥化を阻害するなどの難点があった。
【０００５】
【発明が解決しようとする課題】本発明は、従来の編地袋に上記の如き難点があったことに鑑みて為されたもので、縫製箇所が全く無く安価で丈夫な生分解性を有する簡易丸編み袋を提供することを技術的課題とするものである。
【０００６】
【課題を解決するための手段】本発明は、上記の技術的課題を解決するために、筒状の丸編生地から成る袋胴部１と、この袋胴部１の端部の生地同士を接合した袋底部２とから成る丸編み袋であって、この袋底部２が、袋胴部１の端部に予め編み込まれてある、当該袋胴部１を構成する糸よりも低融点の溶着糸を加熱溶着せしめることによって袋胴部１の端部を溶着接合して形成されており、かつ、これら袋胴部１の構成糸および溶着糸が生分解性高分子を含んでいるという技術的手段を採用した。
【０００７】ここで、生分解性高分子とは、自然界の土壌中や淡水・海水中に生存する微生物や生体酵素によって比較的容易に分解され、その分解生成物が生態系に無害である高分子材料をいうものであり、水切りゴミ袋の構成素材として使用できる程度の耐水性を有するものであれば、特に限定されるものではなく、例えば、ポリエチレンサクシネート、ポリエチレンアジペート等の脂肪族ポリエステル、ポリ乳酸、ポリカプロラクトン等のオキシカルボン酸やラクトンのポリエステル、微生物が自然界で作るポリ－３－ヒドロキシバリレート、ポリ－３－ヒドロキシブチレート、ポリ－３－ヒドロキシカプロレート等の微生物ポリエステル等を挙げることができ、これらの単独または二種以上を配合して使用することができる。
【０００８】
【発明の実施の形態】以下、本発明を添付図面に示す実施形態に基づいて詳しく説明する。なお、図１は本発明に係る生分解性簡易丸編み袋の全体斜視図、図２～図４は同生分解性簡易丸編み袋の製造方法を示す製造工程図、図５及び図６は同生分解性簡易丸編み袋の他の製造方法を示す製造工程図である。
【０００９】図１に示す本実施形態の生分解性簡易丸編み袋Ｈは、流し台の排水口やバスケット（通称三角コーナー）に装着可能な水切りゴミ袋として具体化されている。
【００１０】図１中、符号１で指示するものは、本実施形態の生分解性簡易丸編み袋Ｈの袋胴部であり、この袋胴部１は、生分解性高分子から成る糸を丸編みした筒状の丸編生地から構成されている。本実施形態では、生分解性を備えたポリエチレンサクシネート糸（昭和高分子株式会社製「ビオノーレ（登録商標）＃1000」、融点114℃）を平編組織で筒状に編成した伸縮自在な丸編生地を採用しており、この袋胴部１の袋口部10は、予め仮縒りした生分解性ポリ乳酸繊維（カネボウ合繊株式会社製「ラクトロン」）を丸編みして拡縮自在になっている。
【００１１】図１中、符号２で指示するものは、本実施形態の生分解性簡易丸編み袋Ｈの袋底部であり、この袋底部２は、生分解性を有し低融点の溶着糸を加熱溶融して袋胴部１の端部の生地同士を溶着固定して構成されている。即ち、ポリエチレンサクシネート糸から構成された袋胴部１の端部には予め、当該ポリエチレンサクシネート糸よりも低融点の生分解性を備えた溶着糸Ｍが、当

該ポリエチレンサクシネート糸の組織に同時に編み込まれており（図２参照）、かかる溶着糸Ｍのみを加熱溶融せしめることによって袋胴部１の端部の生地同士（ポリエチレンサクシネート糸同士）を溶着固定して袋底部２が構成されているのである。なお、本実施形態では溶着糸Ｍとして生分解性を備えたポリエチレンサクシネート・アジペート糸（昭和高分子株式会社製「ビオノーレ（登録商標）＃3000」融点95℃）を採用している。

【００１２】このように、本実施形態の生分解性簡易丸編み袋Ｈにあっては、丸編生地Ｆの生地同士を溶着糸で溶着固定して袋底部２を構成しているので、従来の編地ゴミ袋のように手間の掛かる縫製処理を一切行わずとも簡単に製袋することができ、極めて安価な水切りゴミ袋を提供することができるのである。

【００１３】また、本実施形態の生分解性簡易丸編み袋Ｈは、袋胴部１を構成している構成糸そのものを溶融させるのではなく、低融点の溶着糸Ｍのみを加熱溶融させることによって袋底部２を形成しているので、この袋胴部１を構成している構成糸の熱履歴による強度低下等の品質劣化を回避することが可能となり、しかも、この袋胴部１の構成糸を取り囲んで固化した溶着糸Ｍが袋胴部１の端部を確実に固定するので、極めて丈夫な水切りゴミ袋を提供することができるのである。

【００１４】また、本実施形態の生分解性簡易丸編み袋Ｈは、袋胴部１を構成する構成糸および袋底部２を形成する溶着糸Ｍが、生分解性高分子から構成されているので、微生物等によって容易に分解されることになり、厨芥等の生ゴミを袋ごと土中に埋めたり、堆肥化装置に入れても、土中や堆肥化装置中で完全に分解され、袋内の生ゴミの堆肥化を阻害することもない。また、この生分解性簡易丸編み袋Ｈの袋胴部１は編み組織を成していて優れた水分透過性を有しているので、微生物等による分解を促進することができ、比較的短期間に分解、堆肥化することができるのである。

【００１５】なお、本実施形態では、この袋底部２を、袋胴部１の端部の生地同士を殆ど襞を形成させることなく単に重ね合わせるようにして溶着糸Ｍで溶着接合して構成しているが、本発明はこれに限定されるものではなく、図６に示すように、袋胴部１の端部の生地を局部的に収束させた状態で溶着糸により溶着接合して袋底部２を形成するようにしても良い。このように、袋胴部１の端部の生地を収束させて溶着固定すれば、袋底部２がより丈夫になる。

【００１６】本実施形態の生分解性簡易丸編み袋Ｈは、次の製造方法によって製造される。図２～図４を参照しながら説明する。

【００１７】まず、図２に示すように、周知の丸編み機を用いて、両端部に伸縮自在な耳組織Ｓ・Ｓを有し、長手方向における中間部位に、他部位を構成している糸よりも低融点の溶着糸Ｍが編み込まれた筒状の丸編生地Ｆを編成する。この丸編生地Ｆを構成する構成糸及び溶着糸Ｍは生分解性高分子を含んでいる。

【００１８】そして、図３に示すように、この丸編生地Ｆの中間部位を加熱し、この低融点の溶着糸Ｍのみを溶融させ、この溶着糸Ｍが丸編生地Ｆを構成する糸を取り囲んだ状態で当該溶着糸Ｍを冷却固化せしめることにより、丸編生地Ｆの中間部位の生地同士を溶着接合する。

【００１９】然る後、図３中の符号Ｃで指示するように、この溶着糸Ｍによる溶着接合部を切断して丸編生地Ｆを二分割することによって、図４に示すように、筒状の丸編生地から成る袋胴部１と、この袋胴部１の端部を溶着糸で溶着接合した袋底部２とから成る簡易丸編み袋Ｈが製造されるのである。

【００２０】このように、本実施形態の生分解性簡易丸編み袋Ｈの製造方法にあっては、丸編生地Ｆの生地同士を溶着糸Ｍで溶着接合してから切断するので、切断処理が簡単であると共に、両端部に耳組織Ｓを有する丸編生地Ｆから同時に二つの生分解性簡易丸編み袋Ｈを製造することができるので、生分解性簡易丸編み袋を効率的に量産することができ、生産性が向上して生分解性簡易丸編み袋を安価に提供することが可能なのである。

【００２１】なお、上記実施形態の製造方法にあっては、丸編生地Ｆの中間部位の生地同士を、あまり襞を形成させることなく単に重ね合わせるようにして溶着糸Ｍで溶着接合しているが、これに限定されるものではなく、図５に示すように、丸編生地Ｆの中間部位を局部的に収束させて溶着糸Ｍで溶着接合するようにしても良い。このことによって、図６に示すように、袋胴部１の端部の生地を収束させて溶着固定した袋底部２を備えた丈夫な生分解性簡易丸編み袋Ｈを量産することが可能となる。

【００２２】

【発明の効果】以上、実施形態をもって説明したとおり、本発明に係る生分解性簡易丸編み袋にあっては、丸編生地の生地同士を溶着糸で溶着固定して袋底部を構成しているので、従来の編地ゴミ袋のように手間の掛かる縫製処理を一切行なわずとも簡単に製袋することができ、極めて安価な水切りゴミ袋を提供することができる。

【００２３】また、本発明の生分解性簡易丸編み袋は、袋胴部を構成している糸そのものを溶融させるのではなく低融点の溶着糸を加熱溶融させることによって袋底部が形成されているので、この袋胴部を構成している糸の熱履歴による強度低下等の品質劣化を回避することが可能となり、しかも、この袋胴部の構成糸を取り囲んで固化した溶着糸が袋胴部の端部を確実に固定するので、極めて丈夫な水切りゴミ袋を提供することができる。

【００２４】また、本発明の生分解性簡易丸編み袋は、袋胴部を構成している構成糸及び袋底部を形成する溶着糸が、生分解性高分子を含んでいるので、微生物等によ

って容易に分解されることになり、厨芥等の生ゴミを袋ごと土中に埋めたり、堆肥化装置に入れても、土中や堆肥化装置中で完全に分解され、袋内の生ゴミの堆肥化を阻害することがない。また、この生分解性簡易丸編み袋の袋胴部は編み組織を成していて優れた水分透過性を備えているので、微生物等による分解を促進することができ、比較的短期間に分解、堆肥化することができるのである。

【図面の簡単な説明】

【図１】本発明に係る生分解性簡易丸編み袋の全体斜視図である。

【図２】同生分解性簡易丸編み袋の製造方法を示す製造工程図である。

【図３】同生分解性簡易丸編み袋の製造方法を示す製造工程図である。

【図４】同生分解性簡易丸編み袋の製造方法を示す製造工程図である。

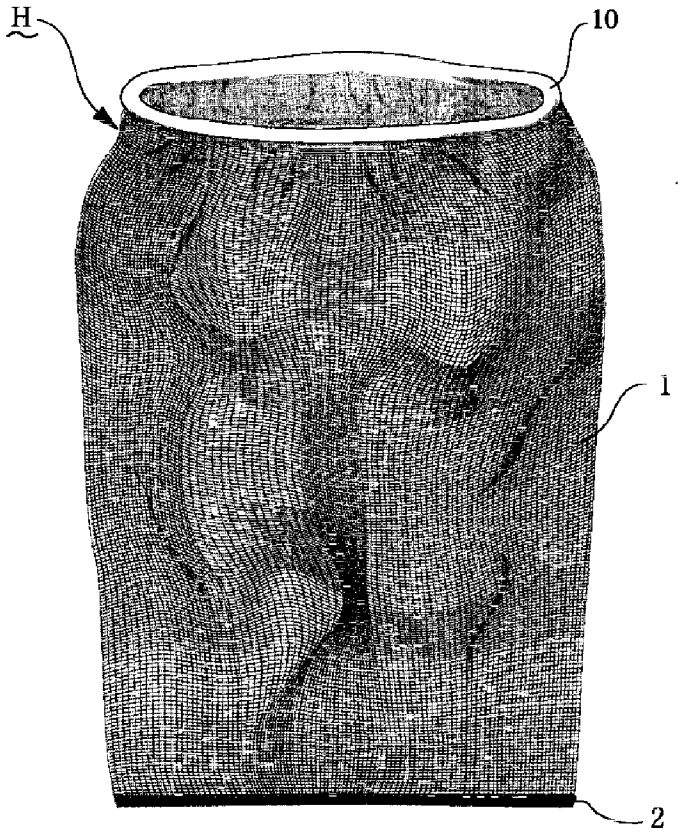
【図５】同生分解性簡易丸編み袋の他の製造方法を示す製造工程図である。

【図６】同生分解性簡易丸編み袋の他の製造方法を示す製造工程図である。

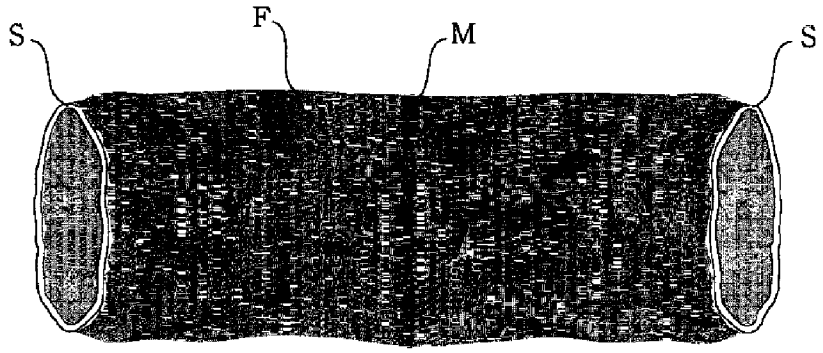
【符号の説明】

1	袋胴部
2	袋底部
F	丸編生地
M	溶着糸

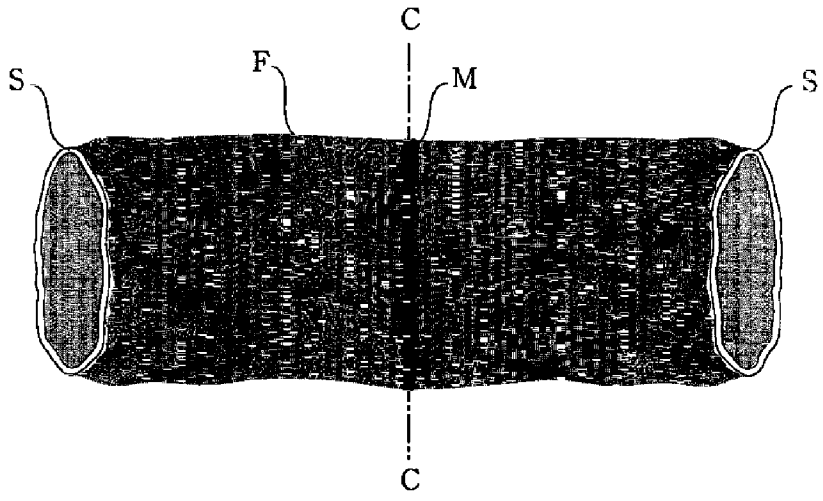
【図１】



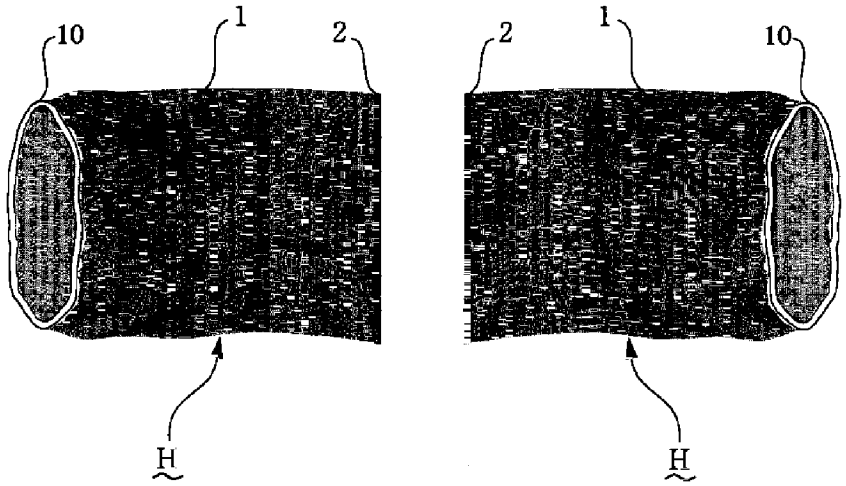
【図2】



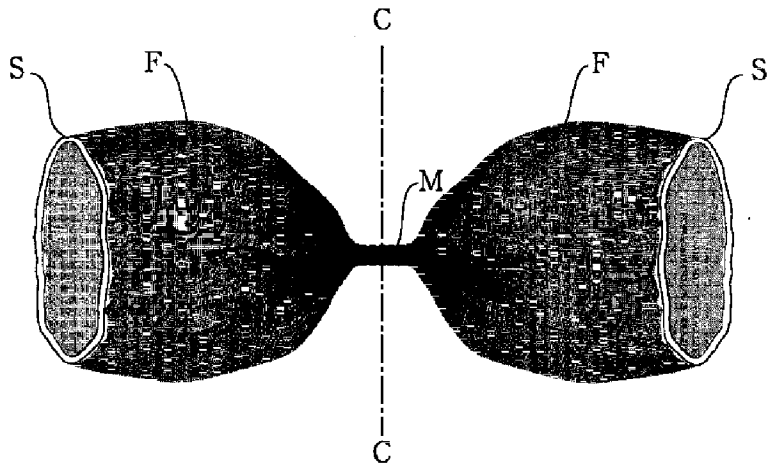
【図3】



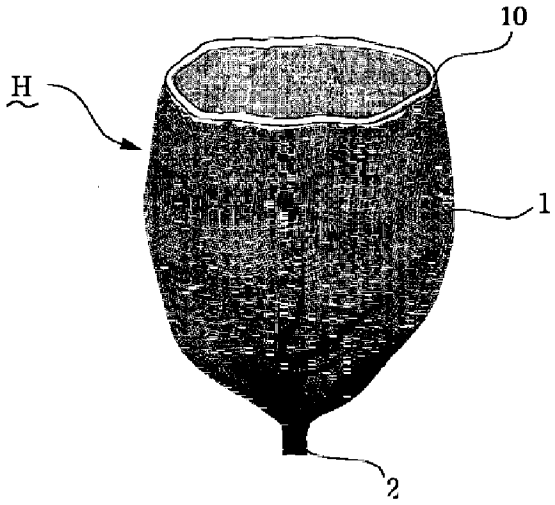
【図4】



【図５】



【図６】



フロントページの続き

(51)Int.Cl.[7]		識別記号	FI		(参考)
B65F	1/00	102	B65F	1/00	102D
D04B	1/22		D04B	1/22	

Fターム(参考) 3E023 FA03 FA10
3E064 AD03 BA21 BB01 BC18 BC20
EA22 FA01 GA06 HM01
3E086 AA23 AB03 AD01 BA04 BA42
BB44 BB51 BB71 BB90 CA40
4L002 AA07 AC00 AC05 BA01 DA00
DA01 EA00 EA02 FA00 FA10

B35

Espacenet

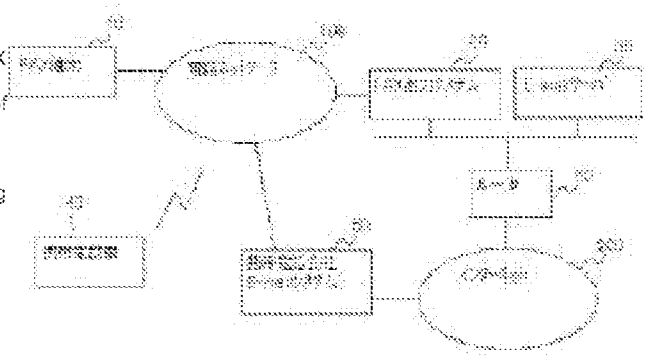
Bibliographic data: JP 2003037632 (A)

SYSTEM AND METHOD FOR ELECTRONIC MAIL ACCESS

Publication date:	2003-02-07	
Inventor(s):	TANIZAWA HIROTAKA +	
Applicant(s):	NEC COMMUNICATION SYST +	
Classification:	**- international:**	***G06F13/00; H04L12/58; H04M11/00; H04N1/00; H04N1/32;*** (IPC1-7): G06F13/00; H04L12/58; H04M11/00; H04N1/00; H04N1/32
	- European:	
Application number:	JP20010225287 20010726	
Priority number (s):	JP20010225287 20010726	
Also published as:	• JP 3730868 (B2)	

Abstract of JP 2003037632 (A)

PROBLEM TO BE SOLVED. To provide a system and a method for electronic mail access, with which the contents of the E-mails can be easily and surely confirmed at the destination of visit by utilizing a FAX and a portable telephone set or the like. SOLUTION: A FAX terminal 10, a portable telephone set 40 and a FAX output system 20 are connected through a telephone network 100, an E-mail server 30, an E-mail system 50 of a portable telephone company and the FAX output system 20 are connected through the Internet 200 and the FAX output system has at least a means for receiving electronic mails transmitted to the prescribed user of the E-mail server, a means for extracting the titles from the electronic mails, a means for preparing the list of titles, a means for transmitting the list to the portable telephone sets,, and a means for outputting the contents of the reply mails of the list or electronic mails designated by the user on a telephone line to prescribed FAX terminals designated by the user.



Last updated:
26.04.2011 Worldwide
Database 5.7.22; 93p

(19)日本国特許庁（ＪＰ）　(12)**公開特許公報**（Ａ）　(11)特許出願公開番号
特開2003－37632
（P2003－37632A）
(43)公開日　平成15年２月７日(2003.2.7)

(51)Int.Cl.[7]		識別記号	FI		テーマコード(参考)	
Ｈ０４Ｌ	12/58	１００	Ｈ０４Ｌ	12/58	１００Ｃ	５Ｃ０６２
Ｇ０６Ｆ	13/00	６４０	Ｃ０６Ｆ	13/00	６４０	５Ｃ０７５
Ｈ０４Ｍ	11/00	３０２	Ｈ０４Ｍ	11/00	３０２	５Ｋ０３０
Ｈ０４Ｎ	1/00	１０７	Ｈ０４Ｎ	1/00	１０７Ｚ	５Ｋ１０１
	1/32			1/32	Ｚ	

審査請求　未請求　請求項の数16　ＯＬ　（全　７　頁）

(21)出願番号　特願2001－225287(P2001－225287)

(22)出願日　平成13年７月26日(2001.7.26)

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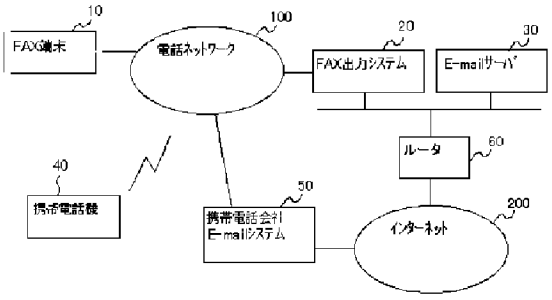
最終頁に続く

(54)【発明の名称】　電子メールアクセスシステム及び電子メールアクセス方法

(57)【要約】
【課題】ＦＡＸ及び携帯電話機等を利用して、Ｅ－ｍａｉｌの内容を外出先で簡便かつ確実に確認することができる電子メールアクセスシステム及び電子メールアクセス方法の提供。
【解決手段】電話ネットワーク１００を介してＦＡＸ端末１０と携帯電話機４０とＦＡＸ出力システム２０とが接続され、インターネット２００を介してＥ－ｍａｉｌサーバ３０と携帯電話会社のＥ－ｍａｉｌシステム５０とＦＡＸ出力システム２０とが接続され、ＦＡＸ出力システムには、Ｅ－ｍａｉｌサーバの所定のユーザ宛に送信される電子メールを受信する手段と、電子メールからタイトルを抽出する手段と、タイトルの一覧表を作成する手段と、一覧表を携帯電話機に送信する手段と、一覧表の返信メール又は電話回線でユーザが指定した電子メールの内容をユーザが指定する所定のＦＡＸ端末に出力する手段とを少なくとも有する。



【特許請求の範囲】
【請求項１】電話網を介して、ＦＡＸ端末と、電子メール送受信機能を備えた携帯端末と、ＦＡＸ出力システムとが接続され、インターネット網を介して、ユーザが第１のアカウントを保有するプロバイダの電子メールサーバと、前記ユーザが第２のアカウントを保有する携帯電話会社の電子メールサーバと、前記ＦＡＸ出力システムとが接続されてなる電子メールアクセスシステムであって、
前記ＦＡＸ出力システムには、前記第１のアカウントに送信される複数の電子メールを受信する手段と、前記複数の電子メールの各々からタイトルを抽出する手段と、抽出した前記タイトルを表示する一覧表を作成する手段と、前記一覧表を電子メールとして前記第２のアカウントに送信する手段と、前記一覧表の中から前記ユーザが選択した電子メールの内容を前記ユーザが指定する所定のＦＡＸ端末に出力する手段とを少なくとも有することを特徴とする電子メールアクセスシステム。
【請求項２】前記一覧表には、少なくとも、前記第１のアカウントに送信された電子メールのタイトルと、各々の前記電子メールに対応づけて採番された通し番号と、ＦＡＸ出力を希望するか否かを示す所定のマーカとが表示されることを特徴とする請求項１記載の電子メールアクセスシステム。
【請求項３】前記ＦＡＸ出力システムに、ＦＡＸ出力を希望する電子メールの内容をＦＡＸ用にイメージ変換する手段を備え、前記電子メールにファイルが添付されている場合に、前記電子メールの本文と前記添付ファイルの内容とが統合されたイメージとしてＦＡＸ出力されることを特徴とする請求項１又は２に記載の電子メールアクセスシステム。
【請求項４】前記ＦＡＸ出力システムに、前記第１のアカウントに送信された電子メールの中から前記携帯端末で送信した前記一覧表の返信メールを選別する手段と、前記返信メールの前記一覧表の中から前記マーカを識別して対応する電子メールを抽出する手段と、前記返信メール中に挿入された出力を希望するＦＡＸ端末の番号を抽出する手段とを備えることを特徴とする請求項１乃至３のいずれか一に記載の電子メールアクセスシステム。
【請求項５】前記ＦＡＸ出力システムに、前記電話網を介して所定の電話機からアクセスするユーザを認証する手段と、該電話機から送信される信号を受信し、前記一覧表の中から前記信号に対応する前記通し番号の電子メールを抽出する手段と、出力を希望するＦＡＸ端末の番号を受信する手段とを備えることを特徴とする請求項１乃至３のいずれか一に記載の電子メールアクセスシステム。
【請求項６】前記携帯端末が、携帯電話機、ＰＨＳ、メール送受信機能を有するノート型パソコン又はＰＤＡのいずれか一からなることを特徴とする請求項１乃至５のいずれか一に記載の電子メールアクセスシステム。
【請求項７】電話網を介して、ＦＡＸ端末と、電子メール送受信機能を備えた携帯端末と接続され、インターネット網を介して、ユーザが第１のアカウントを保有するプロバイダの電子メールサーバと、前記ユーザが第２のアカウントを保有する携帯電話会社の電子メールサーバと接続されるＦＡＸ出力システムであって、
該ＦＡＸ出力システムに、前記第１のアカウントに送信される複数の電子メールを受信する手段と、前記複数の電子メールの各々からタイトルを抽出する手段と、抽出した前記タイトルを表示する一覧表を作成する手段と、前記一覧表を電子メールとして前記第２のアカウントに送信する手段と、前記一覧表の中から前記ユーザが選択した電子メールの内容を前記ユーザが指定する所定のＦＡＸ端末に出力する手段とを少なくとも有することを特徴とするＦＡＸ出力システム。
【請求項８】前記一覧表には、少なくとも、前記第１のアカウントに送信された電子メールのタイトルと、各々の前記電子メールに対応づけて採番された通し番号と、ＦＡＸ出力を希望するか否かを示す所定のマーカとが表示されることを特徴とする請求項７記載のＦＡＸ出力システム。
【請求項９】ＦＡＸ出力を希望する電子メールの内容をＦＡＸ用にイメージ変換する手段を備え、前記電子メールにファイルが添付されている場合に、前記電子メールの本文と前記添付ファイルの内容とが統合されたイメージが生成されることを特徴とする請求項７又は８に記載のＦＡＸ出力システム。
【請求項１０】更に、前記第１のアカウントに送信された電子メールの中から前記携帯端末で送信した前記一覧表の返信メールを選別する手段と、前記返信メールの前記一覧表の中から前記マーカを識別して対応する電子メールを抽出する手段と、前記返信メール中に挿入された出力を希望するＦＡＸ端末の番号を抽出する手段とを備えることを特徴とする請求項７乃至９のいずれか一に記載のＦＡＸ出力システム。
【請求項１１】更に、前記電話網を介して所定の電話機からアクセスするユーザを認証する手段と、該電話機から送信される信号を受信し、前記一覧表の中から前記信号に対応する前記通し番号の電子メールを抽出する手段と、出力を希望するＦＡＸ端末の番号を受信する手段とを備えることを特徴とする請求項７乃至９のいずれか一に記載のＦＡＸ出力システム。
【請求項１２】電話網を介して、ＦＡＸ端末と、電子メール送受信機能を備えた携帯端末と、ＦＡＸ出力システムとが接続され、インターネット網を介して、ユーザが第１のアカウントを保有するプロバイダの電子メールサーバと、前記ユーザが第２のアカウントを保有する携帯電話会社の電子メールサーバと、前記ＦＡＸ出力システムとが接続されてなるシステムを用いた電子メールアク

セス方法であって、
前記ＦＡＸ出力システムにおいて、前記第１のアカウントに送信される複数の電子メールを受信するステップと、前記複数の電子メールの各々からタイトルを抽出するステップと、抽出した前記タイトルを表示する一覧表を作成するステップと、前記一覧表を電子メールとして前記第２のアカウントに送信するステップと、前記一覧表の中から前記ユーザが選択した電子メールの内容を前記ユーザが指定する所定のＦＡＸ端末に出力するステップとを少なくとも実行することを特徴とする電子メールアクセス方法。
【請求項１３】前記一覧表に、少なくとも、前記第１のアカウントに送信された電子メールのタイトルと、各々の前記電子メールに対応づけて採番された通し番号と、ＦＡＸ出力を希望するか否かを示す所定のマーカとを表示することを特徴とする請求項１２記載の電子メールアクセス方法。
【請求項１４】前記ＦＡＸ出力システムにおいて、ＦＡＸ出力を希望する電子メールの内容をＦＡＸ用にイメージ変換するステップを有し、前記電子メールにファイルが添付されている場合に、前記電子メールの本文と前記添付ファイルの内容とを統合したイメージとしてＦＡＸ出力することを特徴とする請求項１２又は１３に記載の電子メールアクセス方法。
【請求項１５】前記ＦＡＸ出力システムにおいて、前記第１のアカウントに送信された電子メールの中から前記携帯端末で送信した前記一覧表の返信メールを選別するステップと、前記返信メールの前記一覧表の中から前記マーカを識別して対応する電子メールを抽出するステップと、前記返信メール中に挿入された出力を希望するＦＡＸ端末の番号を抽出するステップとを有することを特徴とする請求項１２乃至１４のいずれか一に記載の電子メールアクセス方法。
【請求項１６】前記ＦＡＸ出力システムにおいて、前記電話網を介して所定の電話機からアクセスするユーザを認証するステップと、該電話機から送信される信号を受信し、前記一覧表の中から前記信号に対応する前記通し番号の電子メールを抽出するステップと、出力を希望するＦＡＸ端末の番号を受信するステップとを有することを特徴とする請求項１２乃至１４のいずれか一に記載の電子メールアクセス方法。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、電子メールアクセスシステム及び電子メールアクセス方法に関し、特に、ＦＡＸ及び携帯電話を用いて電子メールの内容を確認することができる電子メールアクセスシステム及び電子メールアクセス方法に関する。
【０００２】
【従来の技術】従来、外出先において個人で利用している電子メール（以下、Ｅ－ｍａｉｌと称す）を確認する場合、（１）ノートＰＣ、ＰＤＡ端末などの携帯端末を使い、個人の利用しているサービスプロバイダーからＥ－ｍａｉｌをダウンロードし、ノートＰＣ、ＰＤＡ端末などで確認する、（２）個人のＥ－ｍａｉｌアカウントから携帯電話会社にＥ－ｍａｉｌを転送するように設定し、携帯電話機で確認する、等の方法がとられている。
【０００３】
【発明が解決しようとする課題】しかしながら、（１）の方法の場合には、「ノートＰＣ、ＰＤＡ端末などの携帯端末と携帯電話機または公衆電話等の固定電話回線との接続が必要であり、煩雑な操作を伴う。」、「ノートＰＣ、ＰＤＡ端末などの携帯端末の持ち運びが必要。」、「ノートＰＣのバッテリー寿命が短いものが多い。」等の問題があった。
【０００４】一方、（２）の方法の場合には、「Ｅ－ｍａｉｌを携帯電話機等の小さな画面で確認するために情報の視認性が悪い。」、「携帯電話会社のサービスの制約により大きなサイズのＥ－ｍａｉｌが確認できない。」、「ＰＣのワードプロセッサなどで作られた添付ファイルが確認できない。」、「会社のＥ－ｍａｉｌシステムの場合には携帯電話会社までのメールの転送区間にインターネットを利用するため、セキュリティー上の問題があり、場合によっては会社がメールの転送を禁止している。」等の問題があった。
【０００５】本発明は、上記問題点に鑑みてなされたものであって、その主たる目的は、ＦＡＸ及び携帯電話機等を利用して、Ｅ－ｍａｉｌの内容を外出先で簡便かつ確実に確認することができる電子メールアクセスシステム及び電子メールアクセス方法を提供することにある。
【０００６】
【問題を解決するための手段】上記目的を達成するため、本発明の電子メールアクセスシステムは、電話網を介して、ＦＡＸ端末と、電子メール送受信機能を備えた携帯端末と、ＦＡＸ出力システムとが接続され、インターネット網を介して、ユーザが第１のアカウントを保有するプロバイダの電子メールサーバと、前記ユーザが第２のアカウントを保有する携帯電話会社の電子メールサーバと、前記ＦＡＸ出力システムとが接続されてなる電子メールアクセスシステムであって、前記ＦＡＸ出力システムには、前記第１のアカウントに送信される複数の電子メールを受信する手段と、前記複数の電子メールの各々からタイトルを抽出する手段と、抽出した前記タイトルを表示する一覧表を作成する手段と、前記一覧表を電子メールとして前記第２のアカウントに送信する手段と、前記一覧表の中から前記ユーザが選択した電子メールの内容を前記ユーザが指定する所定のＦＡＸ端末に出力する手段とを少なくとも有するものである。
【０００７】本発明において、前記一覧表には、少なくとも、前記第１のアカウントに送信された電子メールの

タイトルと、各々の前記電子メールに対応づけて採番された通し番号と、ＦＡＸ出力を希望するか否かを示す所定のマーカとが表示されることが好ましい。

【０００８】また、本発明において、前記ＦＡＸ出力システムに、ＦＡＸ出力を希望する電子メールの内容をＦＡＸ用にイメージ変換する手段を備え、前記電子メールにファイルが添付されている場合に、前記電子メールの本文と前記添付ファイルの内容とが統合されたイメージとしてＦＡＸ出力されることが好ましい。

【０００９】また、本発明において、前記ＦＡＸ出力システムに、前記第１のアカウントに送信された電子メールの中から前記携帯端末で送信した前記一覧表の返信メールを選別する手段と、前記返信メールの前記一覧表の中から前記マーカを識別して対応する電子メールを抽出する手段と、前記返信メール中に挿入された出力を希望するＦＡＸ端末の番号を抽出する手段とを備える構成とすることができる。

【００１０】また、本発明において、前記ＦＡＸ出力システムに、前記電話網を介して所定の電話機からアクセスするユーザを認証する手段と、該電話機から送信される信号を受信し、前記一覧表の中から前記信号に対応する前記通し番号の電子メールを抽出する手段と、出力を希望するＦＡＸ端末の番号を受信する手段とを備える構成とすることもできる。

【００１１】また、本発明において、前記携帯端末が、携帯電話機、ＰＨＳ、メール送受信機能を有するノート型パソコン又はＰＤＡのいずれか一からなることが好ましい。

【００１２】本発明のＦＡＸ出力システムは、電話網を介して、ＦＡＸ端末と、電子メール送受信機能を備えた携帯端末と接続され、インターネット網を介して、ユーザが第１のアカウントを保有するプロバイダの電子メールサーバと、前記ユーザが第２のアカウントを保有する携帯電話会社の電子メールサーバと接続されるＦＡＸ出力システムであって、該ＦＡＸ出力システムに、前記第１のアカウントに送信される複数の電子メールを受信する手段と、前記複数の電子メールの各々からタイトルを抽出する手段と、抽出した前記タイトルを表示する一覧表を作成する手段と、前記一覧表を電子メールとして前記第２のアカウントに送信する手段と、前記一覧表の中から前記ユーザが選択した電子メールの内容を前記ユーザが指定する所定のＦＡＸ端末に出力する手段とを少なくとも有するものである。

【００１３】また、本発明の電子メールアクセス方法は、電話網を介して、ＦＡＸ端末と、電子メール送受信機能を備えた携帯端末と、ＦＡＸ出力システムとが接続され、インターネット網を介して、ユーザが第１のアカウントを保有するプロバイダの電子メールサーバと、前記ユーザが第２のアカウントを保有する携帯電話会社の電子メールサーバと、前記ＦＡＸ出力システムとが接続されてなるシステムを用いた電子メールアクセス方法であって、前記ＦＡＸ出力システムにおいて、前記第１のアカウントに送信される複数の電子メールを受信するステップと、前記複数の電子メールの各々からタイトルを抽出するステップと、抽出した前記タイトルを表示する一覧表を作成するステップと、前記一覧表を電子メールとして前記第２のアカウントに送信するステップと、前記一覧表の中から前記ユーザが選択した電子メールの内容を前記ユーザが指定する所定のＦＡＸ端末に出力するステップとを少なくとも実行するものである。

【００１４】すなわち、図１において、個人で利用しているＥ－ｍａｉｌを外出先で確認する方法として、携帯電話機４０のＥ－ｍａｉｌ機能を利用して、個人で利用しているＥ－ｍａｉｌサーバ３０で受信したＥ－ｍａｉｌのタイトル一覧表を携帯電話機４０へのＥ－ｍａｉｌとして送信する。外出先等で緊急に確認したい場合、携帯電話機４０で受信したタイトル一覧表をそのまま返信メールとして利用し、ＦＡＸとして出力したいＥ－ｍａｉｌのタイトル部分にマークを付与し、さらに出力先のＦＡＸ端末１０の電話番号を付与して、Ｅ－ｍａｉｌとしてファクス出力システム２０に返信する。ＦＡＸ出力システム２０は、マークを付与されたタイトルをもつＥ－ｍａｉｌの本文をＦＡＸ端末１０に出力するものである。

【００１５】または、Ｅ－ｍａｉｌによる返信を行わず、Ｅ－ｍａｉｌのタイトル一覧表にタイトル単位に付与された、固有番号（たとえば連番）を電話ネットワーク１００を経由しＦＡＸ出力システム２０にプッシュボタン信号で指定し、その後、出力先のＦＡＸ端末１０の電話番号を指定することにより、該当のＥ－ｍａｉｌの内容をＦＡＸ端末１０に出力するものである。

【００１６】

【発明の実施の形態】本発明に係る電子メールアクセスシステムは、その好ましい一実施の形態において、電話ネットワークを介して、ＦＡＸ端末と電子メール送受信機能を備えた携帯電話機とＦＡＸ出力システムとが接続され、インターネットを介して、ユーザが第１のアカウントを保有するプロバイダのＥ－ｍａｉｌサーバと、ユーザが第２のアカウントを保有する携帯電話会社のＥ－ｍａｉｌシステムと、前記ＦＡＸ出力システムとが接続されて構成され、ＦＡＸ出力システムに、Ｅ－ｍａｉｌサーバの第１のアカウントに送信される電子メールを受信する手段と、複数の電子メールの各々からタイトルを抽出する手段と、抽出したタイトルを表示する一覧表を作成する手段と、一覧表を電子メールとして携帯電話機に送信する手段と、一覧表の返信メール又は電話回線でユーザが指定した電子メールの内容をユーザが指定する所定のＦＡＸ端末に出力する手段とを少なくとも有するものであり、ユーザは携帯電話機で第１のアカウントに送信された電子メールのタイトルを確認することがで

き、また、その中から指定した電子メール及び添付ファイルの内容を紙で確認することができる。

【００１７】

【実施例】上記した本発明の実施の形態についてさらに詳細に説明すべく、本発明の一実施例に係る電子メールアクセスシステム及び電子メールアクセス方法について、図１及び図２を参照して説明する。図１は、本実施例の電子メールアクセスシステムの全体構成を示す図であり、図２は、Ｅ－ｍａｉｌタイトルの一覧表の例を示す図である。

【００１８】図１に示すように、本実施例のＦＡＸ出力システムは、ＦＡＸ端末１０と、ＦＡＸ出力システム２０と、Ｅ－ｍａｉｌサーバ３０と、携帯電話機４０と、携帯電話会社Ｅ－ｍａｉｌシステム５０と、それぞれの機器を相互に接続するための電話ネットワーク１００と、インターネット２００と、ルータ６０とから構成されている。なお、本システムの利用者Ａは会社のＥ－ｍａｉｌシステムとして、Ｅ－ｍａｉｌサーバ３０にアカウントＡを所有している。また、携帯電話機４０を所有し、携帯電話会社Ｅ－ｍａｉｌシステム３０にアカウントＢを所有しているものとする。以下に各構成要素について説明する。

【００１９】ＦＡＸ端末１０は、本システムの利用者Ａが外出先で利用できるＦＡＸ端末である。

【００２０】ＦＡＸ出力システム２０は、Ｅ－ｍａｉｌサーバ３０の持つ個人アカウントに対応して、Ｅ－ｍａｉｌ本文とＥ－ｍａｉｌに添付されたＰＣのワープロソフトなどの添付文書ファイルをＦＡＸイメージに変換し、ＦＡＸ端末１０に電話ネットワーク１００を通して出力する機能を有する。また、それぞれのＥ－ｍａｉｌサーバの個人アカウントごとに到着したＥ－ｍａｉｌのタイトル一覧表を、携帯電話機４０を含む最寄りの電話機から電話ネットワーク１００を通したプッシュ信号指示により、Ｅ－ｍａｉｌサーバ３０、ルータ６０、インターネット２００、携帯電話会社Ｅ－ｍａｉｌシステム５０、電話ネットワーク１００を介して携帯電話機４０のＥ－ｍａｉｌとして送出する機能を有する。

【００２１】Ｅ－ｍａｉｌサーバ３０は、利用者Ａが常に利用しているの会社のＥ－ｍａｉｌシステムであり、ルータ６０を介してインターネット２００に接続されている。

【００２２】携帯電話会社Ｅ－ｍａｉｌシステム５０は、たとえば「NTT DoCoMo」が提供しているi-Modeサービスのような、携帯電話機にＥ－ｍａｉｌを表示させるサービスを提供する装置であり、携帯電話機４０に対するＥ－ｍａｉｌの送受信機能を有する。

【００２３】なお、図２は、利用者ＡがＥ－ｍａｉｌサーバ３０にて受信したＥ－ｍａｉｌの一覧表の一例を示す図であり、便宜的に罫線と表にタイトルを表示している。

【００２４】次に、図１及び図２を参照して、本実施例の動作について詳細に説明する。

【００２５】利用者Ａは、所属する会社のＥ－ｍａｉｌサーバ３０の自分当てのアカウントＡに到着したＥ－ｍａｉｌを確認するために、携帯電話４０からＦＡＸ出力システム２０に電話をする。ＦＡＸ出力システム２０は、例えば音声応答などを用いて、利用者Ａを識別するために利用者コード、パスワードの入力を促し、利用者Ａは携帯電話機４０のダイアルキーからＰＢトーンで自分自身の利用者コード、パスワードを入力する。ＦＡＸ出力システム２０は、利用者Ａの正常な認識を完了すると、サービスコードの入力をうながす。それに対して、利用者Ａは、Ｅ－ｍａｉｌの到着確認のサービスコードを携帯電話機４０から入力する。

【００２６】例えば、図２に示すような１０件のＥ－ｍａｉｌの到着がアカウントＡにあったとすると、ＦＡＸ出力システム２０は、Ｅ－ｍａｉｌサーバ３０から利用者ＡのＥ－ｍａｉｌ１１０件の到着を、携帯電話４０に対して例えば合成音声で通知する。利用者Ａは、ＦＡＸ出力システムに対し、１０件のＥ－ｍａｉｌタイトル一覧を携帯電話会社Ｅ－ｍａｉｌシステム５０のアカウントＢへ送出する旨の指示を携帯電話４０からＰＢトーンで実施する。

【００２７】ＦＡＸ出力システム２０は、図２に示す１０件のＥ－ｍａｉｌタイトル一覧をＥ－ｍａｉｌの本文として、携帯電話会社Ｅ－ｍａｉｌシステム５０のアカウントＢに送出する。利用者Ａは携帯電話会社Ｅ－ｍａｉｌシステム５０のＥ－ｍａｉｌ到着通知機能などで携帯電話機４０へのＥ－ｍａｉｌ到着を確認後、携帯電話機４０で図２に示すような自分当てのアカウントＡに届いたＥ－ｍａｉｌのタイトル一覧の確認ができる。ここからＦＡＸ端末１０に対して目的のアカウントＡに届いたＥ－ｍａｉｌ本文を出力するために２つの方法が選択できる。

【００２８】まず、第１の方法は、携帯電話機４０から直接ＦＡＸ出力システム４０を呼び出して、出力したいＥ－ｍａｉｌのフィールド２０１に書かれた連番を指示する方法である。利用者Ａは、届いたＥ－ｍａｉｌ一覧表からＦＡＸ端末１０で詳細に確認したいＥ－ｍａｉｌのタイトルを確認し、該当のＥ－ｍａｉｌに振られたフィールド２０１の連番を記憶する。

【００２９】そして、利用者Ａは、携帯電話４０からＦＡＸ出力システム２０に電話をし、前記と同様な方法で利用者Ａの利用者認証を実施する。その後、利用者Ａは、ＦＡＸ出力サービス機能を選択し、記憶した連番を指定し、その連番を持つＥ－ｍａｉｌのＦＡＸ端末１０への指示を行う。なお、複数の連番を指定すれば複数のＥ－ｍａｉｌ出力指示も可能である。Ｅ－ｍａｉｌの指定が完了した後、ＦＡＸ端末４０の電話番号を指定する。利用者Ａは携帯電話機４０とＦＡＸ出力システム２

０の接続を解除する。

【００３０】ＦＡＸ出力システム２０は、指定を受けた連番を持つＥ－ｍａｉｌをＥ－ｍａｉｌサーバ３０から取り出して、その内容をＦＡＸイメージに変換する。変換完了後、利用者Ａから指定されたＦＡＸ端末１０の電話番号に電話をかけ、ＦＡＸイメージに変換されたＥ－ｍａｉｌの本文をＦＡＸ端末１０に対して出力する。この一連の動作により、利用者Ａは外出先の最寄りのＦＡＸ端末で、利用者Ａに届いたＥ－ｍａｉｌの内容を紙で確認する事ができる。

【００３１】第２の方法は、携帯電話機４０のもつＥ－ｍａｉｌの返信機能を使い、携帯電話会社Ｅ－ｍａｉｌシステム５０を経由してＦＡＸ出力システム２０にＦＡＸ端末１０へ出力すべきＥ－ｍａｉｌの指示を行う方法である。具体的には、利用者Ａは、携帯電話機４０に届いたＥ－ｍａｉｌのタイトル一覧表を確認後、その内容を含む返信メールを作成し、図２に示すタイトル一覧表メール自身の編集を行う。利用者Ａが確認したいタイトルを見つけた場合、マークフィールド２０２に、例えばチェックマーク‘Ｍ’を付与する（図２の例の場合、連番０２と０７がこれに該当する。）。この操作をＦＡＸ端末４０に出力したいタイトル数分実施後、メールの末尾にＦＡＸ端末４０の電話番号を追加記入する。

【００３２】その後、利用者ＡはＥ－ｍａｉｌサーバ３０のアカウントＡに、この内容を携帯電話会社Ｅ－ｍａｉｌシステム５０を介して送信する。アカウントＡの宛先はタイトル一覧メールの送信元宛先に設定されているため、返信メールを指定した場合、携帯端末４０の機能により自動的に設定される。

【００３３】ＦＡＸ出力システム２０は、一定の周期でアカウントＡに到着したＥ－ｍａｉｌの監視を実施している。アカウントＡに到着した返信メールを取り出し、その返信メールのタイトル一覧から、マーク‘Ｍ’の付与されたタイトルを見つけた場合、Ｅ－ｍａｉｌサーバ３０より該当のＥ－ｍａｉｌを取り出して、その内容をＦＡＸイメージに変換する。変換完了後、利用者Ａからメールで指定されたＦＡＸ端末１０の電話番号に電話をかけＦＡＸイメージに変換されたＥ－ｍａｉｌの本文をＦＡＸ端末１０に対して出力する。

【００３４】携帯電話機のＥ－ｍａｉｌ機能を利用したこの第２の方法においてもこれらの一連の動作により、利用者Ａは外出先の最寄りのＦＡＸ端末で、利用者Ａに届いたＥ－ｍａｉｌの内容を紙で確認する事ができる。

【００３５】

【発明の効果】以上説明したように、本発明の電子メールアクセスシステム及び電子メールアクセス方法によれば、下記記載の効果を奏する。

【００３６】本発明の第１の効果は、外出先でＥ－ｍａｉｌを確認する場合でも、ノートＰＣ、ＰＤＡ端末等の携帯端末が不要になるため、持ち運びをする必要がなくなるということである。従って、それぞれの携帯機器のバッテリー寿命を気にする必要もなくなる。

【００３７】本発明の第２の効果は、携帯電話機または電話回線に接続するノートＰＣ、ＰＤＡ端末等の携帯端末が不要であるため、接続するための煩雑さが全くないということである。

【００３８】また、本発明の第３の効果は、携帯電話機のみの操作でサイズの大きなＥ－ｍａｉｌと、ＰＣのワードプロセッサなどで作られた添付ファイルのＦＡＸによる確認が可能になり、視認性を向上させることができるということである。

【００３９】また、本発明の第４の効果は、携帯電話会社のメールシステムへのメール本文の転送が不要（メールのタイトルの送信のみ）になるため、インターネットもつセキュリティー問題を回避できるということである。

【図面の簡単な説明】

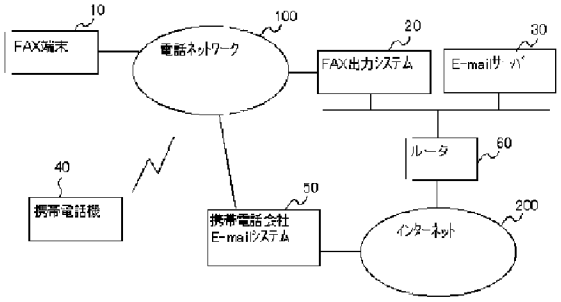
【図１】本発明の一実施例に係る電子メールアクセスシステムの全体構成を示す図である。

【図２】本発明の一実施例に係る電子メールアクセスシステムを用いて送信される電子メールタイトルの一覧の例を示す図である。

【符号の説明】

１０　ＦＡＸ端末
２０　ＦＡＸ出力システム
３０　Ｅ－ｍａｉｌサーバ
４０　携帯電話機
５０　携帯電話会社Ｅ－ｍａｉｌシステム
６０　ルータ
１００　電話ネットワーク
２００　インターネット
２０１　Ｅ－ｍａｉｌのフィールド（連番）
２０１　Ｅ－ｍａｉｌのマークフィールド
２０１　Ｅ－ｍａｉｌのフィールド（タイトル）

【図１】



【図２】

アカウントＡに到着したE-mail一覧

201 通番	202 マーク	203 メールタイトル	送信者	受信日時
０１		会議開催について	田中	00/03/19 9:00
０２	M	機能仕様書の送付	水野	00/03/19 9:11
０３		特許届け出提出締め切り	佐藤	00/03/19 9:22
０４		会議場所の変更について	Jon	00/03/19 10:01
０５		健康診断のお知らせ	金本	00/03/19 12:30
０６		Ａ社システムの納入日変更	中橋	00/03/19 15:42
０７	M	文書の査読依頼	里田	00/03/19 16:18
０８		検討依頼書の送信	島	00/03/19 17:48
０９		承認依頼	諦木	00/03/20 9:02
１０		明日の出社予定時間	武久	00/03/20 9:10

フロントページの続き

Ｆターム(参考)　5C062 AA02 AA12 AA13 AA29 AB38
AC24 AC41 AF00 BA04 BB03
BD09
5C075 AB90 CF05 CF09
5K030 HA06 HB04 HC01 HC09 HC14
HD03 HD06 JT05 JT09 KA01
KA06
5K101 KK01 KK02 LL12 MM07 NN18
UU19